

Exhibit 94

From: Hubbard, Sue (RTM)
Sent: Friday, July 7, 2006 07:40:33 AM
To: Glenn, Robert[RGlenn@crowell.com]
CC: Harrass, Michael (RTM)
Subject: ACGIH

Bob,

On ACGIH, Mike Harrass is leading the team on ACGIH and can bring you up to date

Sue

*Dr Sue Hubbard
Chief Toxicologist
Rio Tinto Minerals
Tel: +44 1483 242055
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*Effective 1st February 2006, Borax is combining its management with two sister companies, namely Luzenac, the world leader in talc and Dampier Salt, the premier exporter of solar salt, to form a new organisation called **Rio Tinto Minerals**. The transition will take place progressively throughout 2006 for full implementation on 1st January 2007.*

Registered Office : Borax Europe Limited 1A Guildford Business Park, Guildford, GU2 8XG. Registered In England No 36374

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-----Original Message-----

From: Glenn, Robert [mailto:RGlenn@crowell.com]
Sent: 30 June 2006 14:02
To: Hubbard, Sue (RTM)
Subject: RE: Publication Update

What is your reaction to ACGIH moving forward with development of a documentation for talc? How are you coming with progress on your notes re our June 13 Meeting? Have Great 4th of July! Sorry, you chaps don't celebrate that one - do you?

Kind regards,

Bob

From: Hubbard, Sue (RTM) [mailto:Sue.Hubbard@borax.com]
Sent: Wednesday, June 28, 2006 5:38 AM
To: Glenn, Robert; Argust, Peter (RTM); TURNER, Eric (LG CIT); Godell, Ralph (LNA); Bernard, Craig (USBORAX); Cutler, Kent (LNA); Keener, Mike (LNA); Yordan, Jorge (LNA); Brown, Judy P. (USBORAX); REFREGIER, Michele (LEU); Harrass, Michael (USBORAX); William G. Kelly, Jr.; Zazenski, Rich (LNA); Hall, Ridgway; Hall, Ridgway
Cc: Metaresearch@hotmail.com; JMuscat@PSU.edu; Hall, Ridgway
Subject: RE: Publication Update

Well done - look forward to getting reprints

Sue

*Dr Sue Hubbard
Chief Toxicologist
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-----Original Message-----

From: Glenn, Robert [<mailto:RGlenn@crowell.com>]

Sent: 27 June 2006 17:46

To: Argust, Peter (RTM); TURNER, Eric (RTM); Hubbard, Sue (RTM); Godell, Ralph (RTM); Bernard, Craig (RTM); Cutler, Kent (RTM); Keener, Mike (RTM); Yordan, Jorge (RTM); Brown, Judy P. (RTM); REFREGIER, Michele (LEU); Harrass, Michael (RTM); William G. Kelly, Jr.; Glenn, Robert; Zazenski, Rich (RTM); Hall, Ridgway; Hall, Ridgway

Cc: Metaresearch@hotmail.com; JMuscato@PSU.edu; Hall, Ridgway

Subject: Publication Update

Ladies and Gentlemen,

I received some fantastic news from Drs. Huncharek and Muscat regarding the manuscripts regarding talc and ovarian cancer which they submitted to the medical literature. First, the manuscript on the meta-analytic study of diaphragm storage in talc and a possible relationship with ovarian cancer has been accepted and will be published in the European Journal of Cancer Prevention. The editor, Carlo LaVecchia, advised Michael by e-mail. Dr. LaVecchia is a prominent figure in cancer prevention and this is an ideal journal in which to have this study appear. Secondly, the review manuscript on the relationship between perineal talc dusting and ovarian cancer has been provisionally accepted and will be published in the Journal of Clinical Epidemiology after minor formatting revisions are made. Another well-respected scientific journal for publication of their manuscript. I know you all join me in commending Michael and Josh for their first-rate study on the talc-diaphragm meta-analysis and their splendid review article on the literature regarding talc and ovarian cancer. We will apprise you as we learn of publication dates for these articles.

Again, thanks Mike and Josh and congratulations!

Kind regards to all,

Exhibit 95

From: Hubbard, Sue (RTM)
Sent: Friday, March 31, 2006 02:07:50 AM
To: Harrass, Michael (USBORAX); Bernard, Craig (USBORAX); Branch, Tracy (USBORAX); Shettle, Keith (RTM); Hoadley, Lara (RTM); Rickards, Helen (RTM)
Subject: FW: Lancet publication of IARC Summaries - Out this morning
Attachments: Lancet Oncology.doc

[More on talc](#)

Sue

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-----Original Message-----

From: Zazenski, Rich (LNA)
Sent: 28 March 2006 20:09
To: Goldberg, Gary (RTM); Parr, Adam (RTM); Keefe, Susan (RTM); Argust, Peter (RTM); JONES, Laura (LEU); Stockman, Mike (USBORAX); Robison, Chris (RTM); Goldsworthy, Denise (DSL); Brown, Judy P. (USBORAX); Sperring, Keith (RTM); TURNER, Eric (RTM); Argust, Peter (RTM); Saperstein, Steve (RTM); Olsen, Jeff (RTM); Hubbard, Sue (RTM)

Subject: Lancet publication of IARC Summaries - Out this morning
Importance: High

To all - Peter asked that I summarize for you the latest developments on the IARC review of talc. This morning, the journal *Lancet Oncology* published a summary of the IARC classifications of Talc, TiO₂, and Carbon Black for IARC Monograph 93. The summary is surprising brief and low key. While it is too early to tell if the release of the summary will garner widespread press coverage, we are cautiously optimistic right now that the release may fly under the radar screen of major news organizations. When you read the summary of the talc/ovarian cancer issue, you'll see that there remains many unaddressed questions.

I've spoken with J&J's Steve Mann and he is also somewhat optimistic - as is their lead attorney John O'Shaughnessy. We'll just have to wait and see what develops in the next few days (Suzi - I forwarded a copy of the Lancet piece to Iris Grossman at J&J - although I haven't heard anything back from her. You might want to give her a call).

Depending on what happens in the coming days and weeks, we'll need to maintain flexibility in our strategy in dealing with the aftermath. For instance, we (J&J with assistance from Luzenac) had plans for Dr. Michael Hunckarek to write a letter to the editor of Lancet taking issue with how the IARC Working Group dealt with the epidemiology studies on talc. As of right now, it looks like we are going to hold off on this due to the many ambiguities in the summary.

We will keep you apprised of any late breaking developments - but so far, so good.

Rich

Exhibit 96

June 30, 2005

William G. Kelly

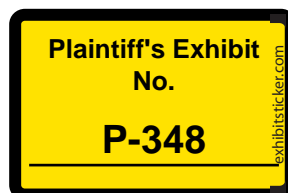
Re: Talc and Ovarian Carcinogenesis

Dear Bill:

Per your request, I have undertaken and completed a systematic discovery of medical scientific experts on the epithelial ovarian carcinogenesis. The objectives of this task were a) to identify such individuals from several disciplines who could be responsible for reviewing the body of scientific literature on talc and ovarian carcinogenesis in order to arrive at an independent and objective conclusion as to whether talc is a likely or definite ovarian carcinogen and b) to form a "priority list" within each discipline based on level of expertise and reputation, research interest and likelihood of objectivity.

Experts were sought in the disciplines of Epidemiology (preferably with background in Biostatistics), Molecular & Cell Biology of Carcinogenesis (emphasizing in vivo models), Pathology, Gynecologic Oncology and General Gynecology. Since all gynecologic oncologists are also board certified in general gynecology and consolidation of manpower is an important consideration, general gynecologists without expertise in gynecologic oncology or the other relevant fields, were not sought.

In addition to personal knowledge of such experts, The National Center for Biotechnology Information (<http://www.ncbi.nlm.nih.gov/>) was used to perform a comprehensive search. Complete and selected bibliographies were then reviewed to identify individuals with appropriate expertise. Some individuals were also identified from the Committee on Cancer Prevention and Control of the Gynecologic Oncology Group (<http://www.gog.org/>) as this important national cooperative group committee has had particular interest in mechanisms of ovarian carcinogenesis and primary prevention. Of the more than two hundred individuals initially identified and screened, a final list of 21 was generated. Some of these thought investigators/thought leaders have expertise in more than one discipline. I have provided tables for each discipline with a rank order and rationale for the rank order below.



Epidemiology

Rank	Last	First	Degree	Title	Institution	URL
1	Brinton	Louise	PhD	Senior Investigator, Chief - Hormonal and Reproductive Epidemiology Branch Unit Chief, Department of Obstetrics, Gynecology & Reproductive Biology	NCI	http://dceg.cancer.gov/people/BrintonLouise.htm
2	Cramer	Daniel	MD		Brigham & Women's Hospital	http://www.brighamandwomens.org/WRHRprog
3	Risch	Harvey	MD, PhD	Professor, Epidemiology	Yale University	..\..\PDF\Personal\Risch H Biblio.pdf
4	Harlow	Bernard	PhD	Professor, Epidemiology	Harvard School of Public Health	Bernard Harlow, Associate Professor in the Depa
5	Colditz	Graham	MD, PhD	Professor of Medicine, Epidemiologist	Harvard Medical School	Channing Laboratory - Graham A. Colditz, MD,
6	Hankinson	Susan	ScD	Associate Professor of Medicine, Epidemiologist	Harvard Medical School	Channing Laboratory - Susan E. Hankinson, ScD
7	Rodriguez	Carmen		Senior Epidemiologist	American Cancer Society	
8	Daly	Mary	MD, PhD	Senior Member, Population Science Division	Fox Chase Cancer Center	Fox Chase Cancer Center: Mary B. Daly, M.D., J

Rationale for Rank Order (first three candidates):

Louise Brinton is a highly regarded epidemiologist with an important administrative position within NCI, who is highly prolific in epidemiology in general and in the epidemiology of ovarian cancer in particular. She has not participated in any studies related to talc exposure that I can tell, so would likely remain unbiased in this regard. She is also a member of the GOG CPC.

Daniel Cramer is an epidemiologist who I believe received his medical subspecialty training in Obstetrics & Gynecology. He is a highly regarded ovarian cancer epidemiologist with a strong publication list in this area. He was a key investigator in the prospective cohort study of talc exposure and ovarian cancer development. This is the most scientifically reputable epidemiologic study in this area. A key factor in the selection of Dr. Cramer to the short list is his combined experience in gynecology and ovarian cancer epidemiology.

Harvey Risch is an MD, PhD, Professor of Epidemiology at Yale and a world renowned ovarian cancer epidemiologist. Based on his selected publication list, he is also likely to remain unbiased. I have had personal contact with Dr. Risch.

Molecular & Cell Biology of Carcinogenesis

Rank	Last	First	Degree	Title	Institution	City	State	URL
1	Auersperg	Nelly	MD, PhD	Professor of Obstetrics & Gynecology	University of British Columbia	Vancouver		Interdisciplinary V
2	Godwin	Andrew	PhD	Member, Medical Science Division	Fox Chase Cancer Center	Philadelphia	PA	Fox Chase Canc
3	Hamilton	Thomas	PhD	Senior Member, Medical Division	Fox Chase Cancer Center	Philadelphia	PA	Fox Chase Canc
4	Bell	Debra	MD	Associate Professor of Pathology	Harvard Medical School M.D. Anderson Cancer Center	Boston	MA	Pathology Servic
5	Bast	Robert	MD	Professor Senior Member, Population Science	M.D. Anderson Cancer Center	Houston	TX	Robert C. Bast, J
6	Testa	Joseph	PhD	Division Chairman, Department of Molecular	Fox Chase Cancer Center M.D. Anderson Cancer Center	Philadelphia	PA	Fox Chase Canc
7	Mills	Gordon	MD, PhD	Therapeutics		Houston	TX	M. D. Anderson C

Rationale for Rank Order (first three candidates):

Nelly Auersperg is one of the most accomplished and well renowned reproductive scientists in the area of ovarian carcinogenesis and the biology of the surface ovarian epithelium. She is number one, hands down. She is also trained in Obstetrics & Gynecology so functionally covers two categories..

Andrew Godwin is the most accomplished current basic scientist in the area of ovarian carcinogenesis. He is a close colleague and disciple of Thomas Hamilton. His work is truly cutting edge.

Thomas Hamilton is a pioneer in the biology of ovarian carcinogenesis and has experience in several in vivo model systems (similar to Dr. Godwin). He is also one of the only scientist to publish on the basic scientific relationship between talc and ovarian cancer.

Pathology

Rank	Last	First	Degree	Title	Institution	City	State	URL
1	Kurman	Robert	MD	Professor of Pathology & Obstetrics/Gynecology	Johns Hopkins	Baltimore	MD	Gynecologic Pathology
2	Bell	Debra	MD	Associate Professor of Pathology	Harvard Medical School	Boston	MA	Pathology Service at MGH
3	Cho	Kathleen	MD	Professor of Pathology & Internal Medicine	University of Michigan	Ann Arbor	MI	University of Michigan - D
4	Orsulic	Sandra	PhD	Assistant Professor, Molecular Pathology	Massachusetts General Hospital	Boston	MA	Pathology Service at MGH

Rationale for Rank Order:

Robert Kurman is a double boarded pathologists and obstetrician-gynecologist who is an icon of ovarian cancer pathology. His CV speaks for itself.

Debra Bell is a molecular pathologist with expertise on carcinogenesis of epithelial ovarian tumors. She is Associate Professor in the Department of Pathology at Harvard Medical School and trained under Dr. Scully, the father of ovarian pathology.

Dr. Cho is a Professor of both Pathology and Internal Medicine with a large body of experience in ovarian cancer pathology. She has several basic scientific interests including the molecular classification of ovarian carcinomas. I know Dr. Cho personally and she is not only well respected, but well spoken.

Dr. Orsulic is also a molecular pathologist from a good institution, with a more limited C.V. than Dr. Bell, but with important expertise in mouse models of ovarian carcinogenesis.

Gynecologic Oncology

Rank	Last	First	Degree	Title	Institution	City	State	URL
1	Berchuck	Andrew	MD	Professor of Obstetrics & Gynecology Associate Professor,	Duke University	Durham	NC	Duke University IGSP Site -- Ar
2	Brewer	Molly	MD, DVM, MS	Obstetrics & Gynecology, Gynecologic Oncology Associate Professor, Obstetrics & Gynecology,	University of Arizona	Tuscon	AZ	University of Arizona, Departme
3	Burger	Robert	MD	Gynecologic Oncology	University of California, Irvine	Orange	CA	ROBERT ALLEN BURGER, MD

Any of these would be excellent, though I am obviously biased in including myself in this list.

Andrew Berchuck is probably the most highly regarded combination of gynecologic oncologist and basic ovarian cancer researcher. Although most of his work has dealt with ovarian carcinogenesis as it relates to molecular genetics, he is a key thought leader in the general subject of epithelial ovarian cancer pathogenesis. He is also president-elect for the Society of Gynecologic Oncologists and a personal colleague. He is not only brilliant and analytical, but extremely classy and well spoken individual.

Molly Brewer is a gynecologic oncologist at U of A with a focused research interest in precursors of ovarian carcinoma development. She is highly involved in primary prevention studies.

Robert Burger is a gynecologic oncologist with a research program dedicated to ovarian cancer pathogenesis and therapeutics. He is a member of several important committees in the Gynecologic Oncology Group, including the Ovarian Cancer Committee, the Committee on Experimental Medicine, and the Developmental Therapeutics Committee. He has an academic interest in ovarian carcinogenesis and prevention, including multiple invited lectures on this subject and organizing and directing a symposium on this subject at his local NCI comprehensive cancer center.

Exhibit 97

To: IMA-NA Talc Section

From: Mark Ellis, President

Re: Marshalling Talc Industry Resources for IARC Monograph 93

Date: August 15, 2005

Background

During its teleconference on August 11, 2005, the Industrial Minerals Association – North America (IMA-NA) Talc Section, in collaboration with the Industrial Minerals Association – Europe (IMA-EU) and the Cosmetic, Toiletry, and Fragrance Association (CTFA), discussed how the talc industry should mobilize its resources to inform the International Agency for Research on Cancer (IARC) Working Group deliberating the carcinogenicity of non-asbestiform talc. The Talc Section requested IMA-NA staff to summarize the subject of their discussions in a short paper, outlining the pros and cons of each activity, and offering an estimate of prospective costs associated with each activity. IMA-NA Talc Section members, and IMA-EU and CTFA staff, agreed to forward the options paper to their principals to determine which activities were of most interest and highest priority, which activities should be funded, and how to the cost of those activities should be allocated. The IMA-NA Talc Section, and collaborating organizations, will discuss their priorities and the commitment of resources during a teleconference scheduled for Thursday, August 18, at 9:30 a.m. (EDST). The consensus of the group was that time was of the essence in resolving a course of action so that necessary steps could proceed apace.

Activities

The discussion revolved around four identified activities: 1) formation of a talc industry task force to assemble documentation and arguments to support talc during the deliberations of the IARC Working Group; 2) collaboration with the International Carbon Black Producers Association (ICBPA) and the American Chemistry Council's Titanium Dioxide Panel (ACC TiO₂ Panel), whose primary products also are the subject of Monograph 93; 3) retention of one or more industry observers to represent the talc industry at the February 2006 meeting of the Working Group in Lyon, France; and 4) initiation of scientific research studies that reasonably could be completed and published, or accepted for publication, in peer-reviewed journals before the February 2006 meeting of the Working Group. Each of these activities is summarized below.

Formation of a Talc Industry Task Force

During its teleconference meeting on July 15, 2005, the IMA-NA Talc Section, and collaborating organizations, agreed to form a talc industry task force to assemble documentation and arguments to support talc during the deliberations of the IARC Working Group. The following individuals were identified as task force participants: Eric Turner (Luzenac); Rich Zazenski (Luzenac); Mike Larson (Minerals Technologies) Ed de Beus (Mondo Minerals); Linda Loretz (CTFA); Michelle Wyart-Remy (IMA-EU) and Mark Ellis (IMA-NA). The first activity of the



task force is to assemble the pertinent scientific literature expected to be considered by the Working Group. The task force is composed of member volunteers and association staff, affording a pool of talc industry expertise utilizing sweat-equity contributions. Staff time and travel are the likely costs associated with this activity.

Talc Industry Collaboration with the ICBPA and ACC TiO2 Panel

For the past several months, IMA-NA staff and company representatives have been holding regular teleconferences with representatives of the ICBPA and ACC TiO2 Panel. Each of the interest groups has provided updates on scientists they were encouraging to self-nominate as potential Working Group members or, alternatively, as Invited Specialists. The collaborators also have discussed whom they might nominate as industry observers and how the organizations representing the three substances under review in Monograph 93 might best coordinate their activities with common purpose. The collaborators have agreed to hold a meeting in Arlington, VA, on September 13, 2005, to brief each other on the issues underlying their primary products and to determine areas of commonality and divergence relative to the Working Group. Staff time and travel costs are expected to be minimal. However, Luzenac has underwritten the participation of Bob Glenn in teleconferences to date, and the cost of his past and continued participation in this activity cannot be viewed as minimal. The collaboration has the potential for future cost savings by pooling activities of the organizations that would otherwise be required independently, such as maintaining a “war room” in Lyon, France, during the meeting of the Working Group.

Industry Observers to Represent the Talc Industry

Under IARC procedures industries with substances under review by IARC are invited to nominate individuals for credentialing as Industry Observers at the Working Group meeting. Unlike Working Group members, Industry Observers have a limited role and no vote in the deliberations of the Working Group. IARC has defined the scope of activities for Industry Observers (see attached *IARC Observer Guidelines*), but they typically have played a significant role in their interactions and contributions to the deliberations of the Working Group. Their acceptance often is a factor of the expertise, utility and congeniality they bring to the Working Group’s deliberations. Unlike Working Group members, or Invited Specialists, IARC provides no financial support for industry observers. Nominees are expected to be self-sustaining (financially supported by outside sources). During last week’s teleconference Talc Section members determined that it was premature to identify specific individuals to nominate to serve as Industry Observers. It was agreed that the talc industry should examine the make-up of the Working Group, as determined by IARC, and evaluate whether any of the scientists the talc industry was encouraging to self-nominate as potential Working Group members or, alternatively, as Invited Specialists were not selected and might make suitable Industry Representatives. Two types of professional expertise were discussed: 1) expertise in evaluating lung overload as a potential mechanism of action in lung cancer, and 2) expertise in evaluating associations between talc exposure and ovarian cancer. Costs associated with retaining an Industry Observer typically would include the cost of their professional consultation (prior to, during, and following the Working Group meeting) and associated travel expenses. It is estimated that the cost of retaining and underwriting an Industry Observer would be \$50,000.

Two Industry Observers would cost on the order of \$100,000. Retention of an Industry Observer(s) to represent the talc industry at the Working Group meeting is regarded as essential to having the ability to monitor, and potentially influence, the outcome of the meeting.

Initiation of Scientific Research Studies

During last week's teleconference Talc Section members considered two proposals for scientific research studies that reasonably could be completed and published, or accepted for publication, in peer-reviewed journals before the February 2006 meeting of the Working Group. Studies completed for consideration by the Working Group also would have utility before the U.S. National Toxicology Program (NTP) should it decide to pursue listing talc in the 12th *Report on Carcinogens*.

RTI Health Solutions (RTI-HS) proposes to update a report entitled *Assessing the Epidemiologic Literature on the Carcinogenicity of Talc*. This report, written in 2000 by Rothman, Pastides, Muscat and Samet, included a meta-analysis (quantitative literature review) of about 20 epidemiologic studies, as well as a meta-regression that examined dose-response trends based on duration and intensity. The original report is viewed as having been instrumental in the decision by the U.S. National Toxicology Program to defer listing talc in the 10th *Report on Carcinogens*. The RTI-HS proposes to bring the literature review up to date and repeat the meta-analysis and meta-regression analyses to evaluate the extent to which recently published studies may have affected the weight of evidence. The study offers the prospect of bringing the most up-to-date information on the critical topic of human epidemiology before the Working Group. The research team is authoritative and highly regarded. However, the consensus of Talc Section members is that the study is overpriced at \$100,000. An effort to reduce the projected cost of the study would be undertaken should the Talc Section be interested in underwriting this research study. The original report by Rothman, *et al.*, and the proposal from RTI-HS are attached (see attached *Rothman – 10th ROC Comments* and *C0205.185 7-5-05*).

Dr. Brooke Mossman, affiliated with the University of Vermont College of Medicine, proposes to compare gene profiling by non-asbestiform talc to that of crocidolite asbestos in human mesothelial and ovarian epithelial cells. Little is known about the cellular and molecular effects of talc on cells. Gene profiling studies have been done on chrysotile asbestos. In contrast to titanium dioxide (a non-pathogenic, control dust), chrysotile induces a number of genes linked to inflammation, fibrogenesis and loss of cell control. Gene profiling increasingly is being used in evaluating the carcinogenic potential of substances. While human epidemiology is likely to be determinative in the Working Group evaluation of talc, studies that demonstrate the absence of a plausible mechanism of action will cast doubt on causal associations between exposure to talc and cancer. Dr. Mossman is a recognized expert in cellular pathology. The projected cost of the study is \$75,000. The proposal from Dr. Mossman is attached (see attached *Talc vs Asbestos 6-30-05*).

Cost Allocation Options

IMA-NA has no institutional formula for allocating the cost of activities pursued by its member sections. Activities pursued by a section, beyond sweat equity and reasonable staff time, are

expected to be self-funded. Thus, it is imperative for Talc Section member companies to determine which activities are of most interest and highest priority, which activities should be funded, and how the cost of those activities should be allocated. Discussion in last week's teleconference suggested that market share might serve as a reasonable basis for allocating the cost of any activities pursued, but antitrust considerations precluded any attempt to discern such a formula under the auspices of IMA-NA. However, IMA-NA staff offered to consult the U.S. Geological Survey (USGS) commodity report for talc to determine if some external source had attempted to make such a determination. However, upon investigation, we learned that USGS has not formally published the market shares of domestic talc producers.

IMA-EU and CTFA, and/or their members, also may be willing to underwrite the cost of any activities determined worthy of pursuit. IMA-EU and CTFA staff have agreed to pursue interest in this regard within their organizations.

Closing Observations

Funding a talc industry initiative to evaluate the carcinogenicity of talc may be a case of: "You can pay me now, or you can pay me later." IARC is viewed around the globe as an authoritative body when it comes to determining the carcinogenicity of chemical substances. An affirmative finding assuredly will follow the product in the future and likely will result in producers of that product being subject to product liability and occupational tort liability actions. The cost of defending these lawsuits, even meritless ones, can be expected to be substantial. An investment at this time to ensure that the existing scientific literature on talc is evaluated appropriately by the Working Group, perhaps resulting in a determination of no, or limited, carcinogenic association could be viewed as a prudent business decision in the long run.

Should you have any questions regarding the contents of this memorandum, please do not hesitate to contact me.

Mark G. Ellis
President
Industrial Minerals Association - North America
4061 Powder Mill Road, Suite 450
Calverton, MD 20705
(301) 595-5550
(301) 595-3303 (Fax)
markellis@ima-na.org

Exhibit 98

Jul. 20. 2006 10:42AM

No. 1573 P. 2



Eric Turner
Vice President, Health, Safety and Environment

July 19, 2006

Mark Ellis
President
Suite 301
Industrial Minerals Association – North America
2011 Pennsylvania Ave. N.W.
Washington, D.C. 20006

Dear Mr. Ellis:

As a follow up to our conversation, I wanted to explain more fully Rio Tinto Minerals' decision to forego any further funding of the University of Vermont talc study (re: "Mossman" study) at this time. I hope that you will share this letter with the members of the talc section as appropriate.

As you know, this study proposal was first brought to Luzenac's attention by Bob Glenn of Crowell & Moring whom we engaged originally during the National Toxicology Program's review of talc and continued through the IARC review. We were prepared to proceed with the Mossman study primarily because there was an excellent chance that the study would be completed and a paper written that could be made available for consideration as part of the formal IARC review in February 2006. We felt that the injection of new data into the talc/ovarian cancer debate could be very helpful. Other talc producers agreed and became interested in sponsoring the project (along with Rio Tinto Minerals) and a collective decision was made to commission the study through the IMA-NA and EUROTALC.

Unfortunately, there were a number of delays that resulted in the postponement of the start of the Mossman project. It became evident in late 2005 that the window of opportunity to have this study completed in time for the IARC review meeting had slipped. When IARC concluded its review and classified "perineal use of talc-based powders" as a Group 2b carcinogen, we began to question the value of proceeding any further with the project. Due to the considerable costs involved and the fact that a key deadline had passed, Rio Tinto Minerals decided that the potential value of this study was greatly diminished and did not warrant any further pursuit at this time.

We would recommend that the talc industry take a step back on this specific effort and review the best way to spend our scarce and precious research dollars. There are upcoming issues that we are monitoring, such as the Cosmetic Ingredients Review and ACGIH® that we as an industry need to focus our attention upon. The time, effort and money required to continue with the Mossman study may be better focused in other areas or efforts.

Luzenac America, 345 Inverness Drive South, Suite 310, Centennial, CO, 80112, Tel +1 303-643-0400, Fax +1 303-643-0446

Jul. 20. 2006 10:42AM

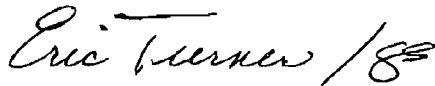
No. 1573 P. 3

Furthermore, the cosmetic and pharmaceutical companies engaged in the business of marketing dusting and body powders to the public have shown no enthusiasm for sponsoring new research on this issue. One of their primary arguments is that one additional study is unlikely to stem the tide of negative sentiment, although those in the industry continue to believe there is no significant risk to product users – supported by the actions of NTP and their withdrawal of talc from its RoC review process. Rio Tinto Minerals finds it problematic to devote additional expenditures for new research in this field when the cosmetic and pharmaceutical companies engaged in this business are reluctant to do so.

We look forward to continuing to address the issues that affect our industry collectively through the IMA-NA and EUROTALC. We have the highest regard for Dr. Mossman and the University of Vermont and have every intention of compensating Dr. Mossman for the work that has been completed to date as was stated in the original agreement.

I appreciate the opportunity to explain this in full.

Sincerely,

A handwritten signature in black ink that reads "Eric Turner" followed by a stylized flourish or date "18".

Eric Turner

Vice President of Health, Safety and Environment

cc: Dr. Michelle Wyart-Remy, Secretary-General, IMA-Europe
Dr. Roger Doome, Senior Scientific Officer, IMA-Europe

Exhibit 99

Fifth Edition
Myths & Facts
about ovarian cancer
What you need to know

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Myths & Facts
about ovarian cancer
What you need to know

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What Is Ovarian Cancer?

Ovarian cancer is a *malignant tumor* (an abnormal, cancerous growth of cells) that can begin in one or both *ovaries* (female reproductive glands). Like all malignant tumors, ovarian malignant tumors are made up of abnormal cells that can divide and reproduce more rapidly than normal cells, that can invade surrounding tissue, and that can travel to other parts of the body through the blood or *lymph vessels* (tubes that carry fluid from connective tissues and between organs), where they develop into secondary tumors. The spread of cancer cells is called *metastasis*.

The ovaries are located within the pelvic cavity, where they are difficult to feel. Also, there are no specific symptoms for ovarian cancer. Therefore, by the time a patient feels or senses that there is a problem or a physician performs tests and diagnoses the condition as ovarian cancer, most malignant ovarian tumors have spread to other areas within the abdomen. By this time, the malignant ovarian tumor usually has caused *ascites*, a build-up of fluid within the abdomen, which leads to abdominal swelling. In fact, abdominal swelling is the reason given by most women diagnosed with ovarian cancer for first consulting with their doctors.

Ovarian cancer is the sixth most common non-skin cancer among women in the United States. Every female born in the United States has a risk of 1 in 55, or 1.8%, of developing ovarian cancer in her lifetime. The risk increases substantially for women with a family history of ovarian cancer. Ovarian cancer is more common in women over age 60, but often occurs in women with a family history before or during their early 40s. Ovarian cancer causes more deaths than any other type of gynecologic cancer and accounts for 5% of all cancer deaths among women.

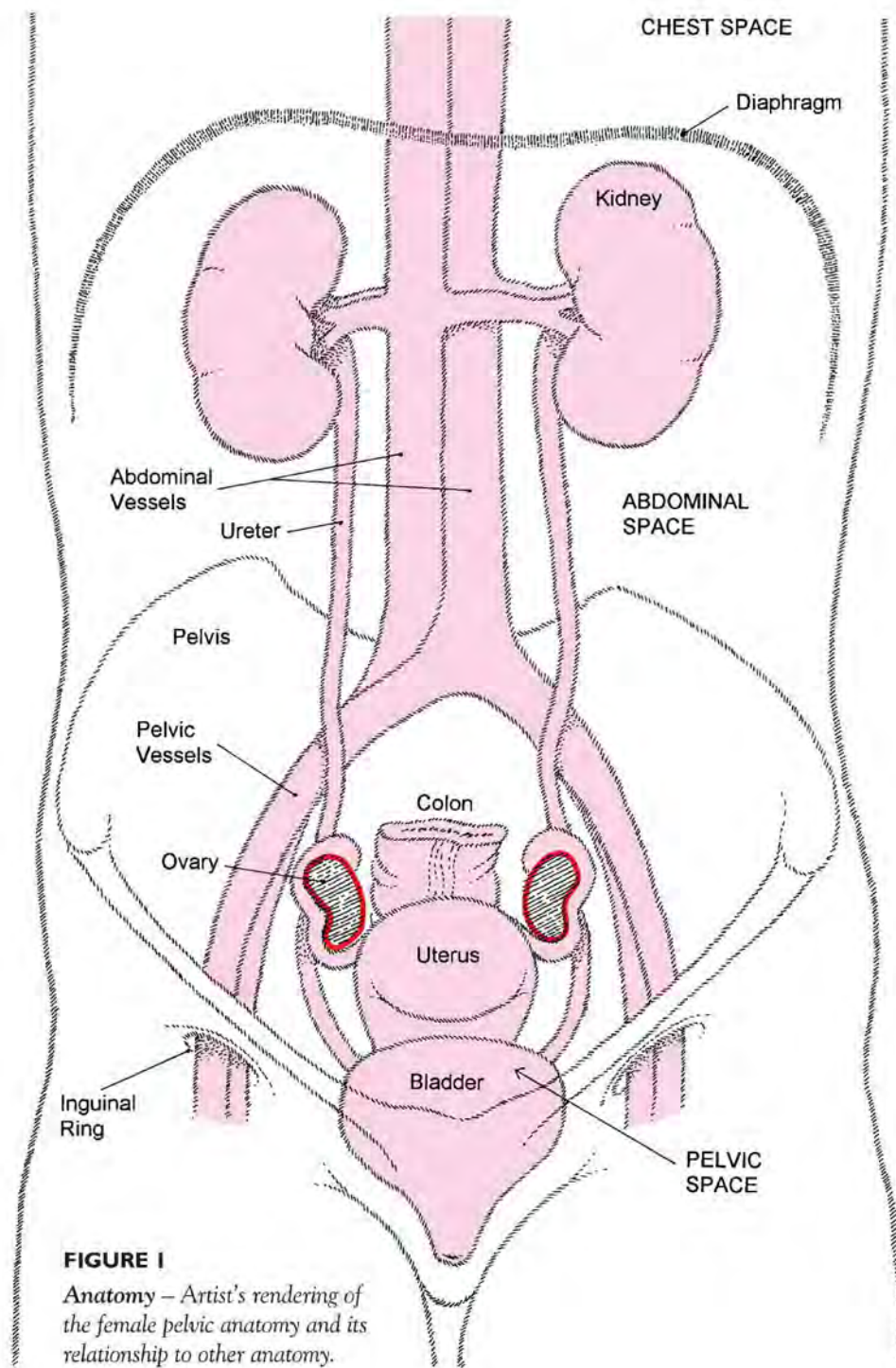
Myth

Ovarian cancer is ovarian
cancer is ovarian cancer.

Fact

There are more than
30 different types of
ovarian cancer.

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TYPES OF OVARIAN CANCER

Ovarian cancer is a very complex disease. There are more than 30 different types, which are classified according to the type of cell from which they start. Malignant ovarian tumors can originate from the *surface epithelium* (cells covering or lining the ovaries), *germ cells* (cells that are destined to form eggs), or *sex cord-stromal cells* (cells that secrete hormones and connect the different structures of the ovaries).

Common Epithelial Tumors: Common epithelial tumors that start in the surface epithelium account for 90% of ovarian cancer cases. These include the following types:

- *Serous tumors.* This most common type of ovarian cancer, accounting for about 40% of common epithelial tumors, occurs most often in women between 40 and 60.
- *Endometrioid tumors.* These tumors account for 20% of common epithelial tumors, and are associated with endometriosis in 5% of the cases and *endometrial carcinoma* (cancer of the womb) in 20% of the cases. Most patients are between 50 and 70.
- *Mucinous tumors.* Mucinous tumors account for about 1% of common epithelial ovarian cancer, and most often affect women 30 to 50.
- *Clear cell carcinoma.* These tumors account for 6% of common epithelial tumors, and most often affect women between 40 and 80.
- *Brenner tumors.* These tumors are uncommon, accounting for between 2% to 5% of common epithelial tumors. Most of these tumors are noncancerous.
- *Undifferentiated tumors.* The remaining 15% of common epithelial cancers are referred to as undifferentiated tumors because their exact cell of origin cannot be determined under a microscope.
- *Borderline ovarian tumors.* These ovarian tumors of low malignant potential are a subgroup of common epithelial tumors that occur in 10% to 15% of cases. These tumors are between cancerous and noncancerous in nature and could be of the serous, endometrioid, mucinous, or clear cell type. They originate on



My response to chemotherapy doesn't depend on the type of ovarian cancer.



For reasons not yet known, serous, endometrioid, and undifferentiated carcinomas respond best to standard chemotherapy for ovarian cancer. Clear cell and mucinous carcinomas have the worst response.

Myth

If it does not run in my family, I cannot get ovarian cancer.

Fact

Genetic or hereditary causes of ovarian cancer account for only 5% to 10% of the estimated 23,400 cases of ovarian cancer diagnosed each year in the United States. The cause or causes of the other 90% are not known.

the surface of the ovary, but do not invade the substance of the ovary. They have a better prognosis (prediction about the possible outcome of a disease) and cure rate than invasive ovarian tumors.

Germ Cell Tumors: Germ cell tumors account for about 5% of all ovarian cancer cases. These tumors can occur in women at any age, but peak incidence is seen during the early 20s. *Dysgerminoma* is the most common germ cell tumor, accounting for 50% of all germ cell tumor cases. About 20% of cases are diagnosed during pregnancy, and 80% occur in women under 30. *Endodermal sinus tumors* (also known as *yolk sac tumors*) are the second most common germ cell tumor, accounting for 20% of all cases, and are common in girls and young adults (average age: 19). Less common germ cell tumors are *embryonal carcinoma*, *immature teratoma*, *choriocarcinoma*, *polyembryomas*, and *mixed germ cell tumors*.

Sex Cord–Stromal Tumors: Sex cord–stromal tumors account for about 5% of ovarian cancer cases. *Granulosa cell tumors* and *Sertoli-Leydig cell tumors* are the most common. Unlike patients with common epithelial tumors, in which 75% are considered to be at Stage III or IV at diagnosis, patients with these tumors are at Stage I at diagnosis 70% of the time (see “Stage and Grade” in the next section). Also unlike common epithelial tumors, sex cord–stromal tumors often have more specific symptoms. *Granulosa cell tumors* are more common in postmenopausal women. These tumors may cause vaginal bleeding and an elevated level of the tumor marker *inhibin* in the blood. *Sertoli-Leydig cell tumors* are rare; the average age of patients diagnosed with these tumors is 25, and only 10% of patients are over 50. About 33% of these tumors produce signs of *virilism* (infrequent menstrual periods, cessation of menstrual periods before menopause, hoarse voice, and appearance of facial hair).

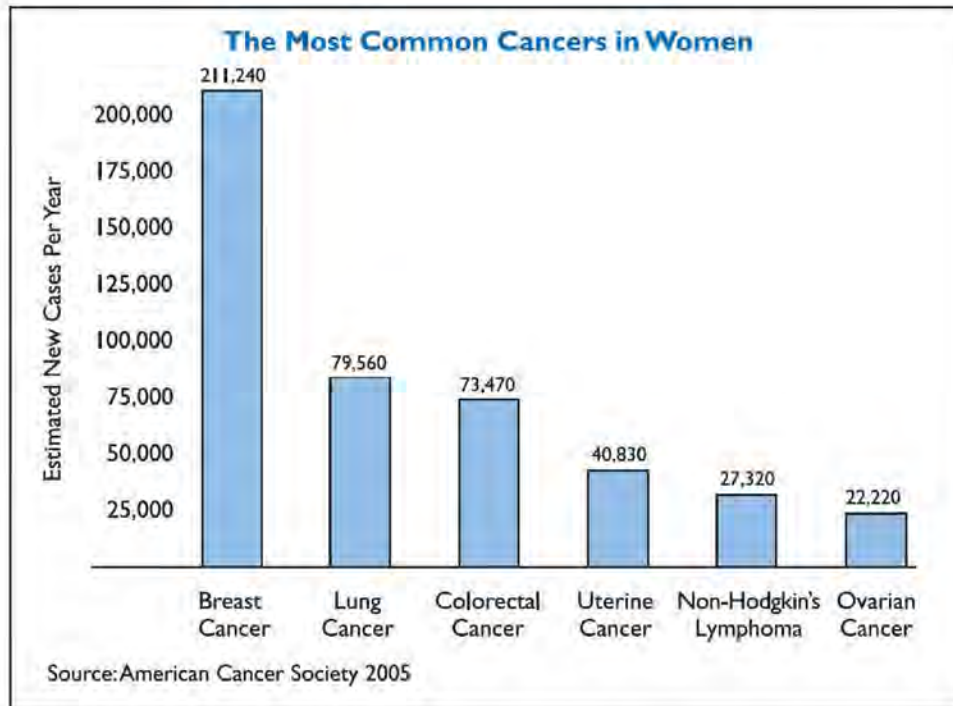


FIGURE 2

The most common cancers in women.

STAGE AND GRADE

Determining the stage and grade of malignant ovarian tumors at diagnosis is important in planning treatment. *Stage* refers to how far the disease has spread. Accurate staging can only be done during a *laparotomy* (any surgical procedure which involves opening the abdominal cavity) that includes *complete surgical staging*. During this surgical procedure, the ovarian tumor is removed, abdominal fluid is collected, and biopsy samples for microscopic examination are taken from the diaphragm, the *omentum* (a fatty, apronlike membrane that hangs down from the stomach and part of the colon in the abdominal cavity), any suspicious nodules in the abdomen, and pelvic and abdominal *lymph nodes* (small glands that filter out bacteria). Based on this surgical assessment, ovarian cancer can be staged as:

Every area of treatment scared me – surgery, chemo, hair loss, nausea. My best advice is to talk to your health care professionals. Ask a lot of questions. It helps to ease your fears.

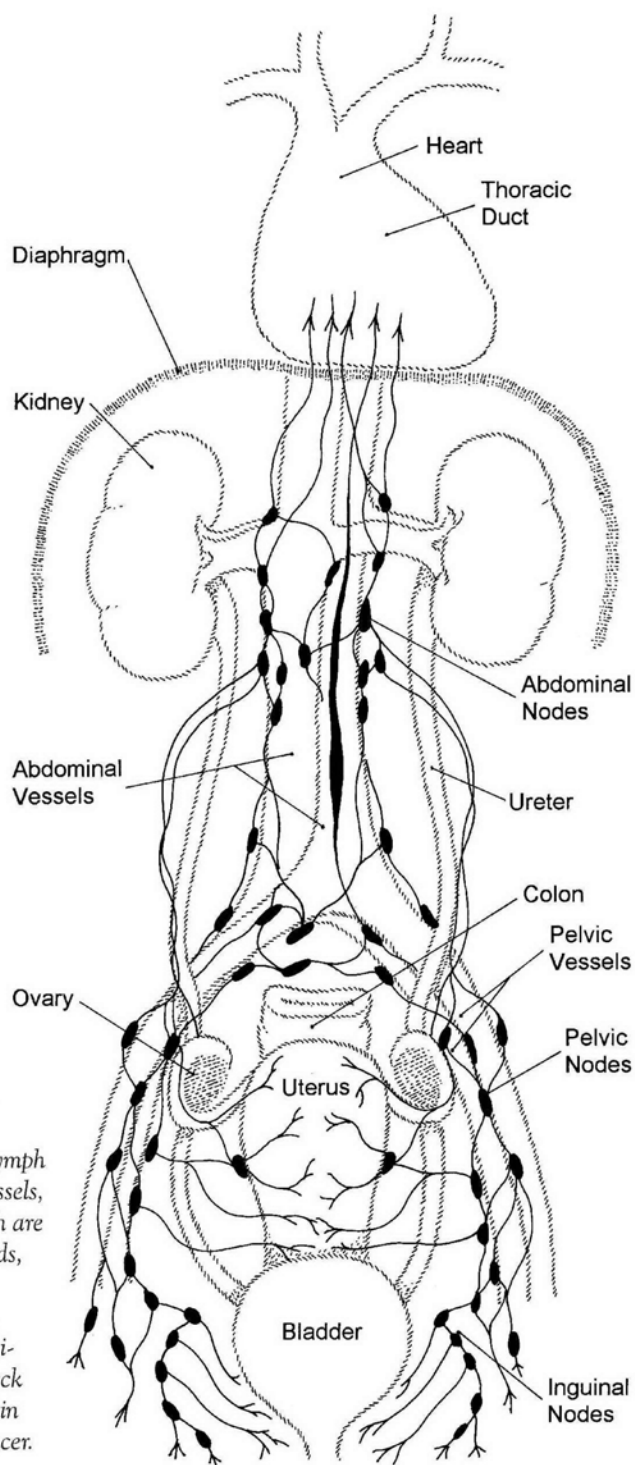


FIGURE 3

Lymph System
– Cancer often spreads via the lymph system (fluid, vessels, and nodes, which are often called glands, as in “She has a swollen gland”). That’s why physicians always check the lymph nodes in the area of a cancer.

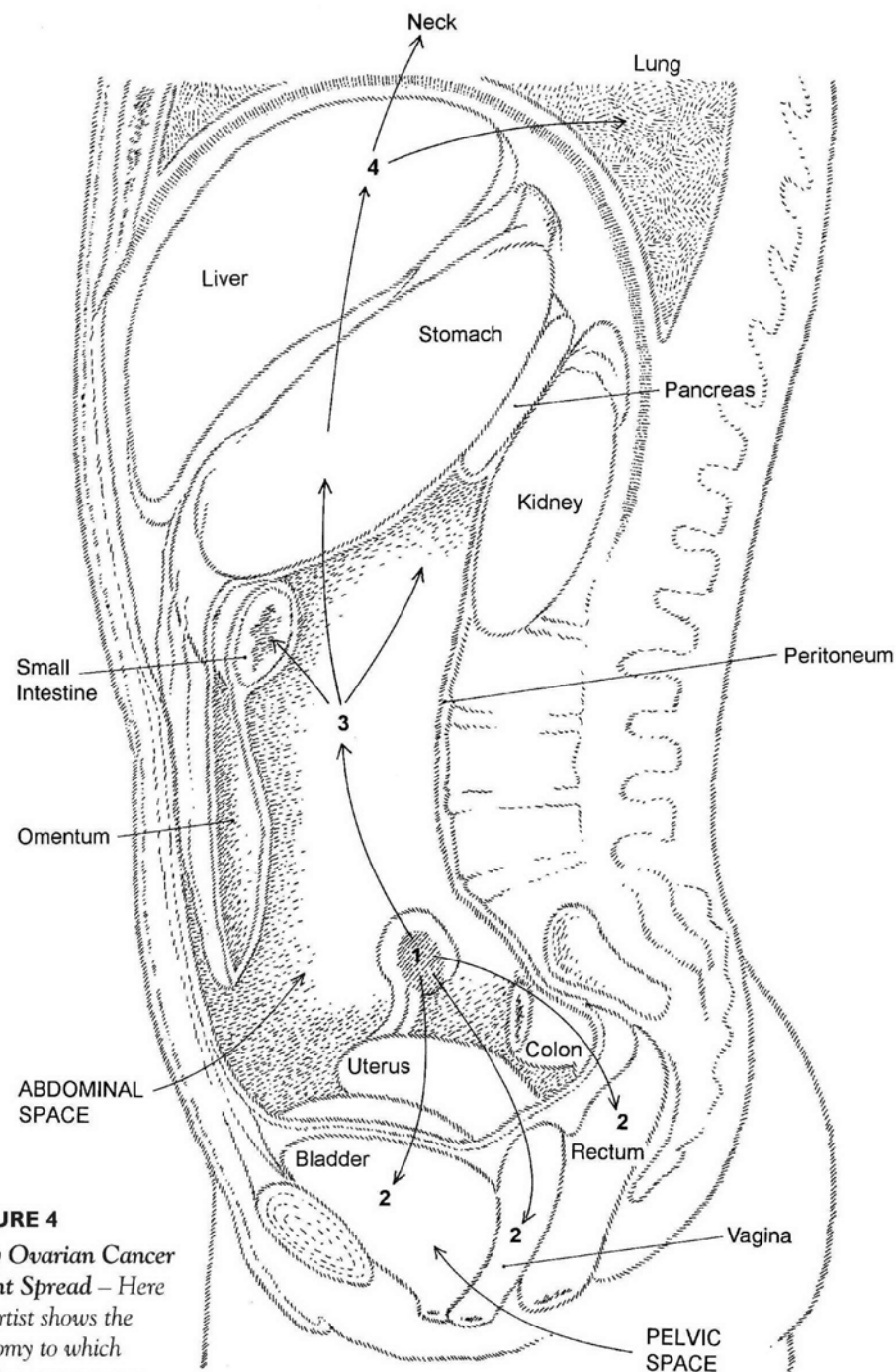


FIGURE 4

How Ovarian Cancer Might Spread – Here the artist shows the anatomy to which ovarian cancer most

commonly spreads (metastasizes). The numbers indicate the stage of disease (the extent to which it has spread). The numeral 1 indicates Stage I disease (disease confined to the ovary), 2 depicts Stage II, 3 indicates Stage III, and 4 depicts Stage IV disease.

Myth

It does not matter what I eat; it can't cause ovarian cancer.

Fact

Several factors related to diet and ovarian cancer are apparent. Ovarian cancer is primarily a disease of middle- and upper-class women from highly industrialized countries (with the exception of Japan); ovarian cancer is very rare in poor countries, such as India and Africa; and one major difference between the highly industrialized countries and poorer countries is the relative high-fat, low-fiber diet in industrialized countries as compared to Africa and India. Japan is a highly industrialized country with a very low rate of ovarian cancer; however, this rate has increased in Japan as the percentage of fat has increased in the Japanese diet. Also, when Japanese women and their daughters move to the United States, their rates of ovarian cancer approach those of women in the United States.

- *Stage I* - Ovarian cancer without spread to any pelvic or abdominal organs;
- *Stage II* - Ovarian cancer with tumor spread to pelvic organs but without spread to the abdomen;
- *Stage III* - Ovarian cancer with tumor spread to abdominal organs; and
- *Stage IV* - Ovarian cancer spread to the lung, liver, or lymph glands in the neck.

The stage of ovarian cancer at diagnosis is also the most important indicator of *prognosis* (prediction of duration, course, and outcome of a disease). Five-year survival rates according to stage as determined by complete surgical staging are 95% for Stage I, 65% for Stage II, 20% for Stage III, and 5% for Stage IV.

Grade refers to the degree of differentiation, or maturity, of the cells forming the malignant ovarian tumor. There are three grades of ovarian cancer cells. Grade 1 is the least malignant (well-differentiated), grade 2 is intermediate (moderately differentiated) and grade 3 is the most malignant (poorly differentiated). Grade 1 tumors grow slowly, and have a better prognosis.

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What Causes Ovarian Cancer?

The specific cause or causes of ovarian cancer are still unknown. All women are at risk for developing this disease. However, several factors have been associated with the development of ovarian cancer, and some of these associations are stronger than others, although research has established that each has at least a small role.

RISK FACTORS

Factors known to increase a woman's chances of developing ovarian cancer include:

Family History of Ovarian Cancer: This is the most important risk factor for developing ovarian cancer. Women with two or more first-degree (mother, sister, daughter) or second-degree (grandmother, aunt) relatives who have had ovarian cancer have up to a 50% risk of developing the disease. The risk also increases if other family members developed ovarian cancer before menopause or if there is a family history of breast, endometrial, colon or rectal cancers in either female or male relatives.

Ovarian cancer can be inherited in three ways: *site-specific familial ovarian cancer*, in which two or more first-degree or a first- and second-degree relative have or had ovarian cancer; *breast-ovarian cancer syndrome*, in which breast and ovarian cancers occur among first- and second-degree relatives; and *hereditary nonpolyposis colorectal cancer syndrome*, in which a family history of colorectal, endometrial, ovarian, or other types of cancer exists in male or female relatives. Women with familial ovarian cancer are usually diagnosed in their early 40s or earlier, as compared to age 61 for women diagnosed with nonfamilial (sporadic) ovarian cancer.

Myth

I shouldn't take fertility drugs because they can cause ovarian cancer.

Fact

Women desiring pregnancy who require fertility-stimulating drugs should be offered them. There are a small number of cases of ovarian cancer in women who have taken fertility stimulating drugs. It is a very small number when compared to the millions of women who have taken fertility stimulating drugs. In fact, in a major report in the *New England Journal of Medicine*, only 5 women who had taken the fertility-stimulating drug clomiphene for more than 12 cycles were found to have a significantly increased risk. This number is exceedingly small when compared to the millions of women who have taken clomiphene.

Myth

Birth control pills (oral contraceptives) cause ovarian cancer.

Fact

The opposite is true; use of oral contraceptives results in a 40% to 50% decrease in the risk of ovarian cancer.

Before I was diagnosed, I was very self-confident—having cancer robs you of that. It's easy to become scared and insecure.

A gene is the functional unit of heredity. Each gene is located at a specific place on a chromosome and is capable of reproducing itself each time the cell divides. The BRCA1 and 2 genes, which are located on chromosomes 17 and 13, respectively, have been genetically linked to the development of ovarian cancer and breast cancer. The normal function of BRCA1 and 2 is thought to be the prevention of these cancers. However, changes in this gene, known as *mutations*, make the gene lose this protective function and predispose a woman to develop ovarian and/or breast cancer. Because genes are passed from parents to their children, the mother-to-daughter transmission of the gene predisposing to ovarian cancer is the most common for familial ovarian cancer. However, fathers can also transmit this gene to their daughters.

Previous Cancers: When a woman is diagnosed and treated for cancer, she is at risk for having another cancer develop in a different body organ. For example, women with ovarian cancer have three times the risk of developing breast cancer, while women with breast cancer have twice the expected risk of developing ovarian cancer.

High-Fat Western Diet: Ovarian cancer is more common in women from industrialized Western countries than in women from other parts of the world. A diet high in meat and animal fat, which is characteristic of industrialized nations, has been linked to the development of ovarian cancer.

Use of Talc (Baby Powder) in the Genital Area: Talc has been implicated in the development of ovarian cancer because it appears in many personal hygiene products and is related to asbestos, a known cancer-causing agent. The theory is that talc particles travel to the ovary through the *cervix* (neck of the uterus), line the uterus and *fallopian tubes* (passage-ways for eggs from the ovaries to the uterus), and result in toxic effects on the ovary.

Never Pregnant/Infertility: Women who have never been pregnant due to infertility and fertile

women who have not had children appear to have an increased risk of ovarian cancer, although there is no consensus on a definitive explanation.

Use of Fertility-Stimulating Drugs: Women taking fertility drugs such as clomiphene citrate (Clomid) and menotropins (Pergonal) to induce ovulation have developed ovarian cancer. However, results from these reports have not inferred a causative relationship between fertility drugs and the development of ovarian cancer.

❖

Myth

Menopausal hormone therapy (estrogen and progesterone) causes ovarian cancer.

Fact

In the 2003 Women's Health Initiative Trial on combined hormone replacement therapy (HRT) there was no statistical increase in ovarian cancer in women on HRT. However, in the 2002 Breast Cancer Detection Demonstration Project report there was a weak association between long-term (10 or more years) estrogen-only hormone replacement therapy and the development of ovarian cancer.

Myth

If my ovaries have been removed surgically, I can still get ovarian cancer.

Fact

Once the ovaries are removed, a woman cannot develop ovarian cancer. A small percentage of women who have had their ovaries removed at the time of hysterectomy for either a noncancerous condition of the uterus or because of a strong family history of ovarian cancer develop a *primary peritoneal carcinoma*, a cancer of the lining of the abdominal cavity. Primary peritoneal carcinoma looks like ovarian cancer under the microscope, acts like ovarian cancer, is treated like ovarian cancer, and responds to treatment like ovarian cancer. However, this condition is not ovarian cancer. Studies have shown that less than 2 in 100 women who have their ovaries removed because of a family history of ovarian cancer will develop primary peritoneal carcinoma.

How Is Ovarian Cancer Diagnosed?

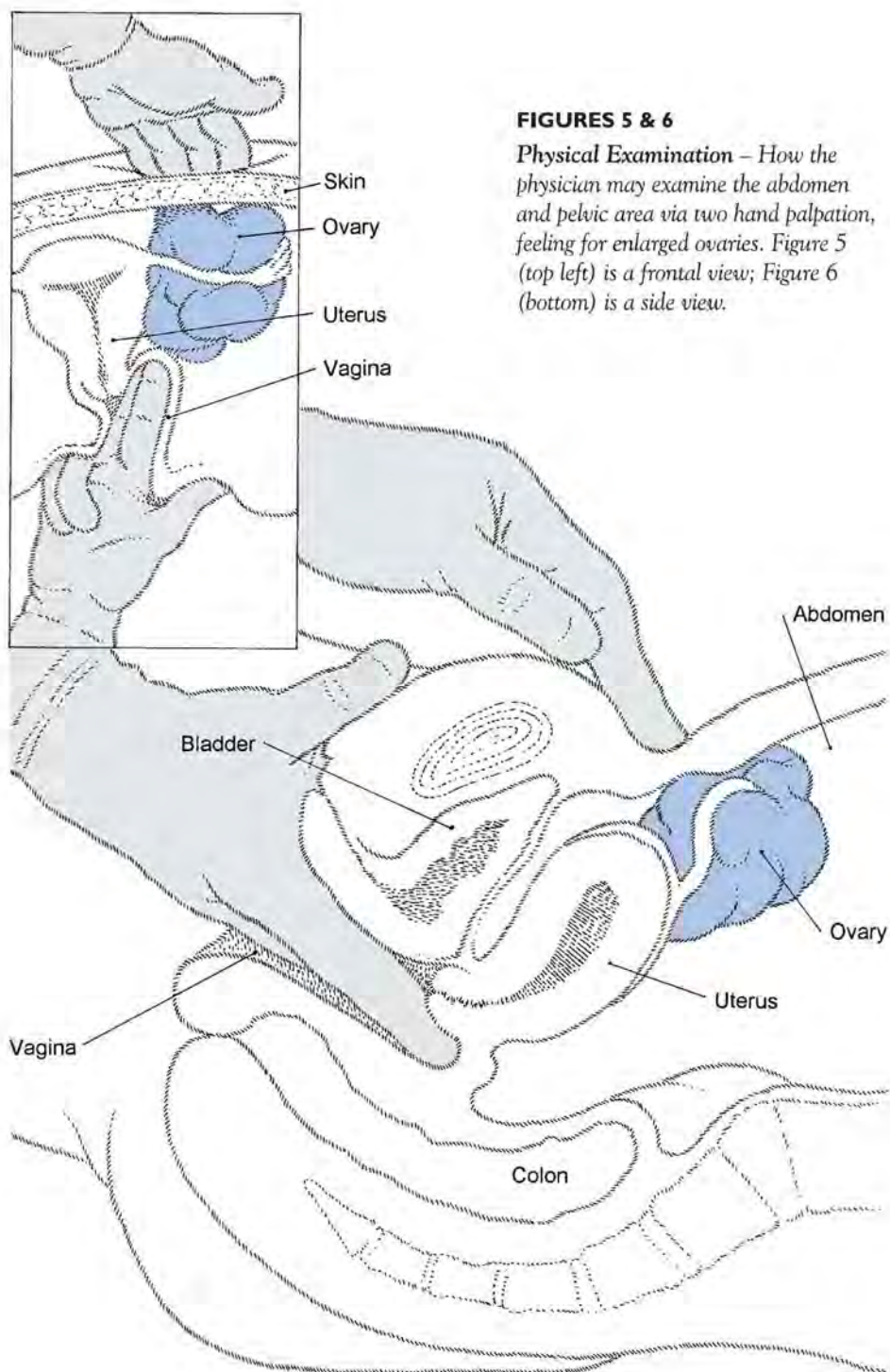
SYMPTOMS ASSOCIATED WITH OVARIAN CANCER

Unfortunately, there are no specific symptoms for ovarian cancer. However, a group of symptoms have occurred in a regular pattern and often enough to be considered symptoms associated with ovarian cancer. These include abdominal swelling, a bloated feeling, vague abdominal and pelvic discomfort, back pain, fatigue, and gastrointestinal symptoms such as gas. True, all women have many of these vague symptoms from time to time. However, if any of these symptoms persists for more than several weeks, this may be an early warning of ovarian cancer. Unfortunately, most women do not consult their gynecologists early enough; as a result, when diagnosed, 75% of patients have ovarian cancer that has spread to other abdominal organs.

PHYSICAL EXAMINATION

Palpating (feeling) a pelvic or abdominal mass on either side of the uterus during a physical examination should suggest suspicion of ovarian cancer. Suspicion should increase if the ovarian cyst or mass is larger than 2 inches (5 cm) in diameter, feels solid rather than cystic (sac-like), is present on both sides, or is found in women past the age of menopause. Feeling nodules on the pelvic floor also should raise suspicion of ovarian cancer, because such a finding usually results from tumor deposits on the *peritoneum* (lining membrane) covering the pelvic floor.

Women with ovarian cancer often have abdominal swelling caused by fluid; a mass caused by a tumor spreading to the omentum can be felt in the upper abdomen. Patients with advanced ovarian cancer sometimes appear malnourished and wasted.



Myth

There are no symptoms when ovarian cancer is limited to the ovary and most curable.

Fact

Although this has always been assumed to be true, in studies that compare the symptoms of women with early localized ovarian cancer to those with nonlocalized, advanced ovarian cancer, the percentage of women who experienced abdominal swelling (clothes getting tighter), abdominal pain, gastrointestinal symptoms, and/or vaginal bleeding or discharge were similar in both groups.

Enlarged glands caused by the spread of the tumor can sometimes be felt in the neck (more often on the left side) or in the groin area.

If the results of the physical examination suggest ovarian cancer, a series of tests should be done to confirm the diagnosis.

DIAGNOSTIC TESTS

Just as there are no specific symptoms for ovarian cancer, there is no one diagnostic test that can confirm the presence of the disease. Rather, doctors must rely on the results of a series of tests as they work through the process of diagnosing ovarian cancer.

CA125 Blood Test: Elevated levels of the protein CA125 in the blood have been associated with ovarian cancer; however, this finding only suggests ovarian cancer, because CA125 levels also are elevated in a number of *benign* (harmless) conditions and during the first trimester of pregnancy. The normal level of CA125 is less than 35 units per milliliter (U/mL) in blood. In general, the higher the level of CA125 found, the greater the chance of having ovarian cancer, especially for women past menopause.

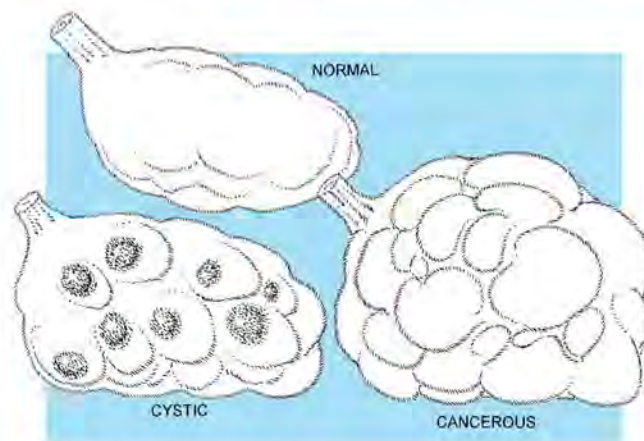


FIGURE 7

Normal and Diseased – Artist's concept of a normal ovary, an ovary containing cysts (fluid-filled nodules), and an ovary containing cancerous cells.



FIGURE 8

Ultrasound Machine – What an ultrasound machine looks like. The vaginal scanner is shown on the side (arrow).

Myth

There are no good tests for diagnosing ovarian cancer in its earliest stages.

Fact

Pelvic exam, the CA125 blood test, and ultrasound are three methods of diagnosing ovarian cancer in women with symptoms suggesting the disease. None of these tests is foolproof when used alone; when used together, however, they can be very helpful in diagnosing ovarian cancer in its earliest stages. In fact, CA125 levels are elevated in 50% of Stage I ovarian cancer patients.

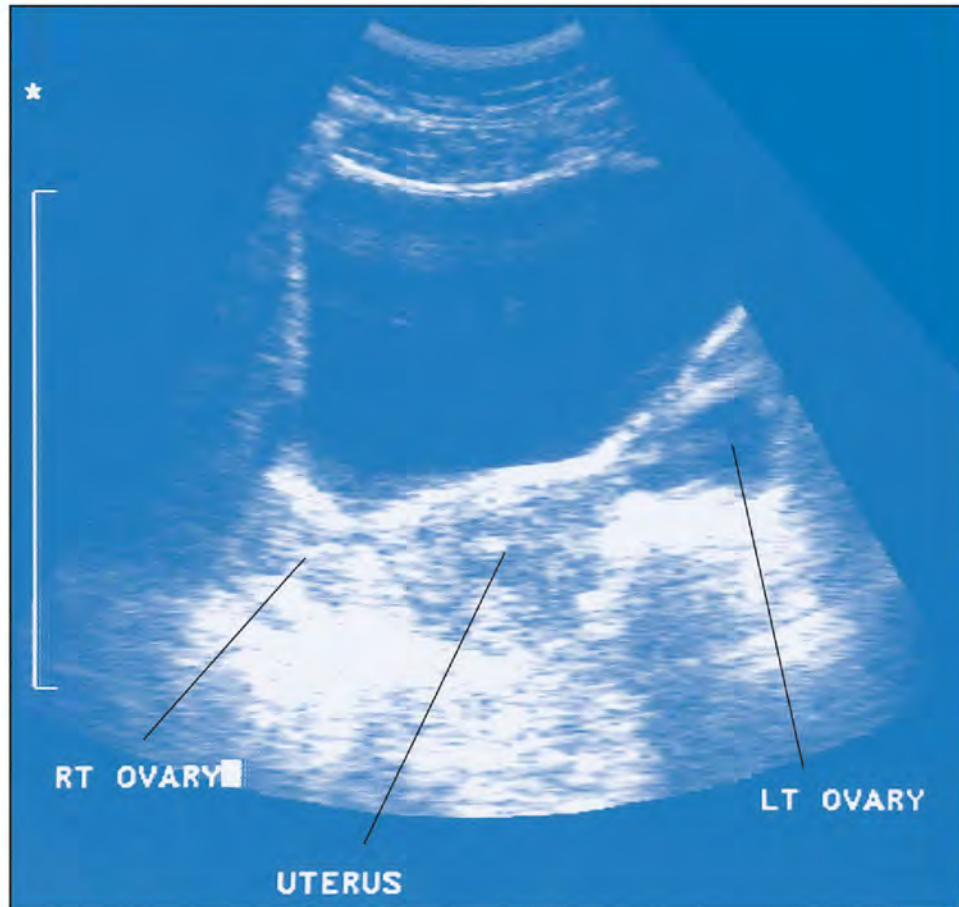


FIGURE 9

An Ultrasound Scan – An ultrasound scan of the lower abdomen shows a full bladder (dark area at top), the ovaries, and the uterus. These ovaries and uterus are normal.

Having cancer is a continuing education process. You learn as you go through treatments.

Ultrasound: This diagnostic tool is the most effective, safest noninvasive method for doctors to use to determine and evaluate the size, shape, configuration, and consistency of the ovaries and to determine whether they are cystic, solid, or both. Ultrasound is based on the principle that solid masses reflect sound waves. High-frequency sound waves are produced by a probe called a *transducer* that is either placed on the abdominal wall (*transabdominal*) over the ovaries or in

the vagina near the ovaries (*transvaginal*). The reflected sound waves are collected and transmitted onto a screen, thus creating a “snapshot” of the pelvis. Transvaginal ultrasound is preferred by most doctors, because the probe can be placed closer to the ovaries and therefore produces improved image quality with better resolution.

Myth

An elevated CA125 level always means that a patient has cancer.

Fact

Although CA125 levels are very useful in diagnosing ovarian cancer and for following the course of treatment, there are many causes of elevated CA125 levels that are not related to cancer, including uterine fibroids, liver disease, inflammation of the tubes and ovaries, endometriosis, and many other types of malignancies.

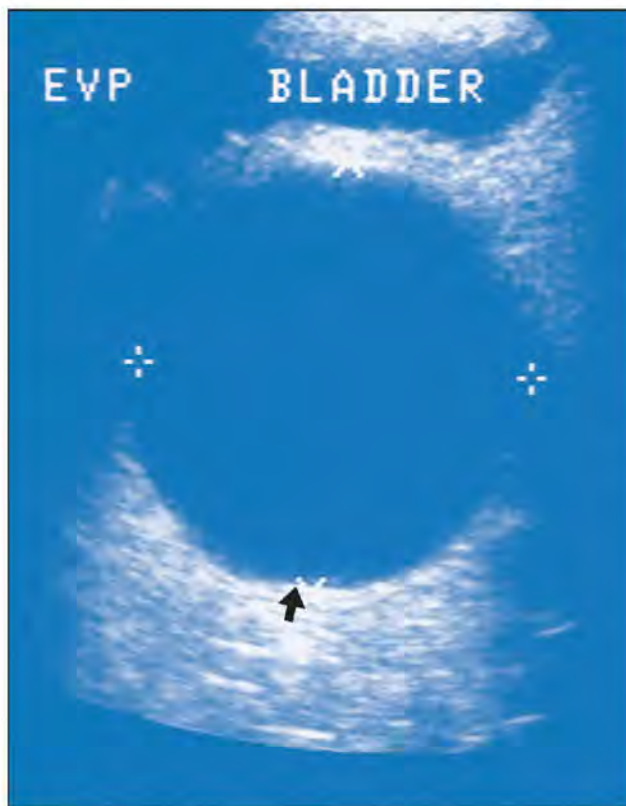


FIGURE 10

An Ovarian Cyst – An ultrasound scan through the lower abdomen showing an ovarian cyst (arrow) behind a full bladder (dark area at top). Sometimes patients are asked to come for imaging with a full bladder because in some circumstances the full bladder will help to obtain more detailed scans. Although this cyst looks large, it actually measures only 4.4 cm by 4 cm (about 1-3/4 inches by 1-1/2 inches). This cyst is completely filled with fluid, which is usually a good sign that the problem is benign, not cancer.

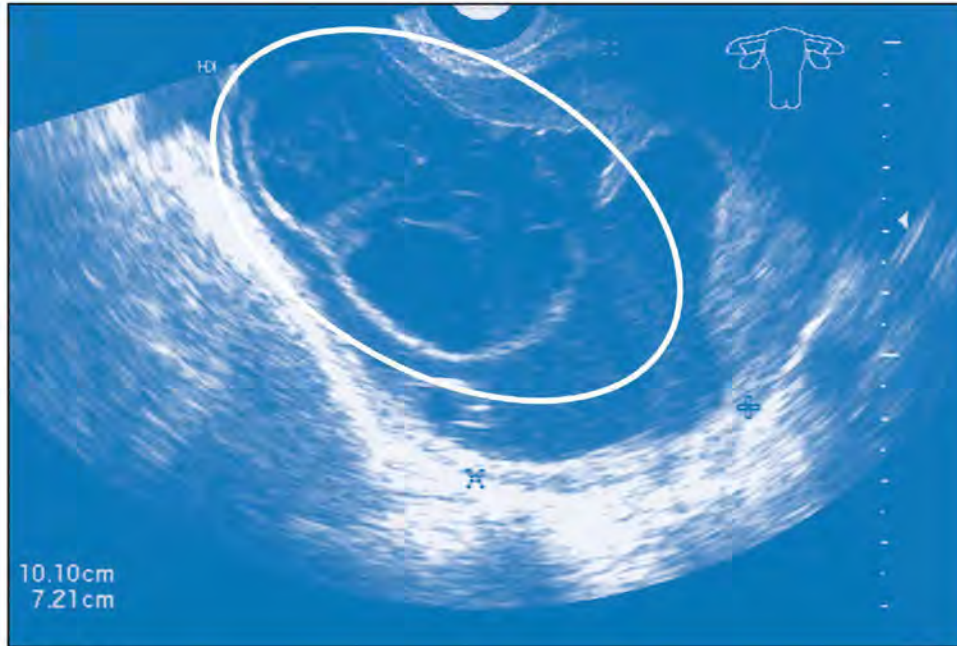


FIGURE II

What a Large Cyst Might Look Like – This vaginal ultrasound scan shows what a large ovarian cyst (circled area) might look like on an ultrasound scan.

I always thought (like everyone else does) that if I was ever diagnosed with cancer, I'd charge the "max" on my credit cards and travel the world. Wrong! You want to fight, you want to beat it!

Transvaginal Color Flow Doppler: However, ultrasound does not provide enough information to determine which abnormal conditions are cancerous and which are not. Transvaginal color flow Doppler is a step forward toward that goal.

Benign ovarian cysts are nourished by normal blood vessels; cancerous ovarian tumors need new blood vessels to supply nourishment for growth. Newly formed tumor blood vessels are smaller and weaker than normal blood vessels and offer very little resistance as blood flows through them. Transvaginal color flow Doppler technology can pinpoint the characteristics of blood vessels supplying the suspicious pelvic mass by using a vaginal probe to measure speed and resistance as blood flows through the vessels. These measurements are recorded and are displayed as graphs showing speed (*pulsatile index*) and amount of resistance (*resistance index*). These indices



FIGURE 12

CAT Scanner – What a computerized axial tomography (CAT) machine looks like. Knowing ahead of time how various diagnostic tools look often eases patients' anxiety.

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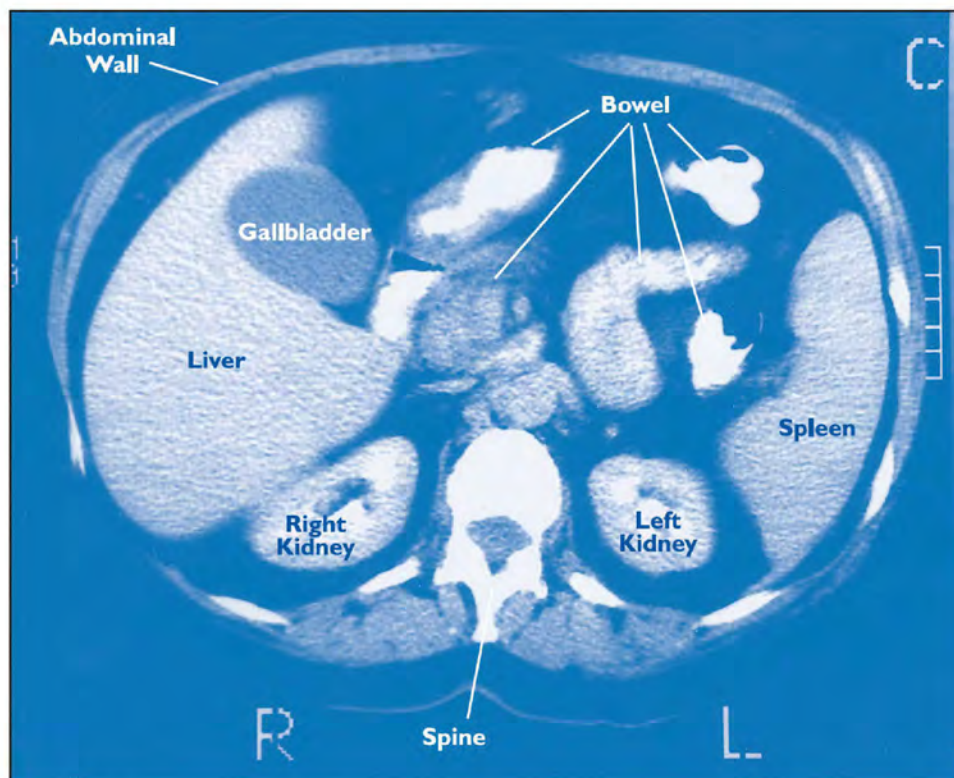


FIGURE 13

Normal CAT Scan – This CAT scan through the upper abdomen shows what a normal liver, gall bladder, loops of small bowel, spleen, and both kidneys would look like on a CAT scan.

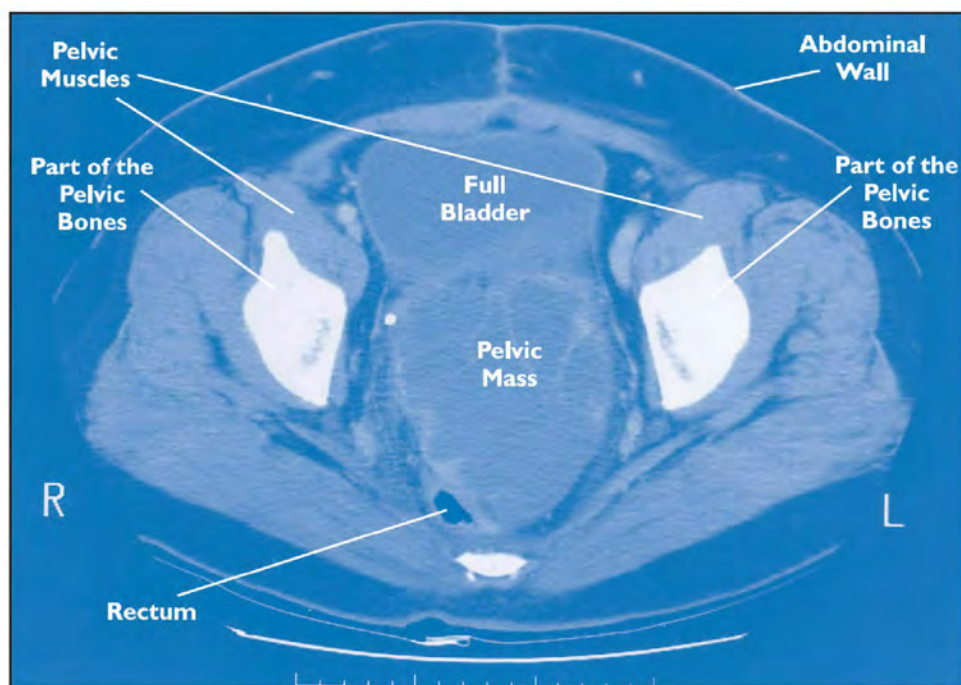


FIGURE 14

Pelvic Mass – A CAT scan through the pelvis demonstrating a pelvic mass behind a full urinary bladder.

Myth

My Pap smear was normal, therefore, I don't have ovarian cancer.

Fact

Papanicolaou, or Pap, smears take cells directly from the cervix and are, therefore, useful in detecting cancer of the cervix. The chance of ovarian cancer cells breaking away from the ovary, being picked up and transferred by the fallopian tube into the uterus, and then being detected on a Pap smear of the cervix approaches zero.

are similar to the diastolic and systolic readings when you have your blood pressure taken. Generally, lower values of either index indicate little resistance to blood flow, suggesting new blood vessels and a cancerous tumor. Similarly, higher values of either index indicate greater resistance, suggesting normal blood vessels and a benign ovarian cyst.

Transvaginal color flow Doppler results aren't perfect, but their accuracy in determining if pelvic masses are cancerous ovarian tumors or benign ovarian cysts is high enough to help the physician decide if surgery might be needed.

CAT Scans: *Computed axial tomography* (CAT) scans may be helpful in diagnosing ovarian cancer. CAT scans use a dye that shows details of the intestines. This method better detects the spread of the cancer into the pelvic and abdominal organs than does ultrasound.

Surgical Biopsy: The only way to confirm the diagnosis of ovarian cancer suggested by the other tests is by taking a biopsy from the ovarian or abdominal tumor during surgery and examining the tissue under a microscope. Laparotomy is the most certain way of diagnosing ovarian cancer and assessing the extent of spread. Other minor surgical procedures that could diagnose ovarian cancer include *aspiration* (removal using suction) of fluid from the abdominal cavity (*paracentesis*) or from around the lungs (*thoracentesis*) using special needles. The fluid removed is treated with chemicals and examined under a microscope. These minor surgical procedures and examination of tissues and fluid can confirm the presence of cancer, but cannot pinpoint the origin of the cancer with certainty.

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How Can Ovarian Cancer Be Prevented?

A number of factors offer women some degree of protection against ovarian cancer. Most have been associated with the *incessant ovulation theory*, which proposes that uninterrupted ovulation causes repeated trauma to the ovary and eventually leads to ovarian cancer. Again, some of these associations are stronger than others. However, research has again established that each has at least a small role. The main prevention factors are:

Oral Contraceptives: Women who use oral contraceptive pills reduce their risk of ovarian cancer by 40% to 50%; the longer oral contraceptives pills are used, the greater the protection.

Pregnancy: Women who have been pregnant have a risk of ovarian cancer that is 30% to 60% lower than that of women who were never pregnant. This protective effect increases with each pregnancy.

Breastfeeding: Research evidence appears to support the role of breastfeeding in protecting women from ovarian cancer.

Tubal Ligation: Women who choose this surgical method of sterilization are at decreased risk of ovarian cancer, although the mechanism is unknown.

Removal of Ovaries: Some women age 40 and over who are about to undergo a hysterectomy for a noncancerous condition involving the uterus, such as uterine fibroids, may decide to have their ovaries removed during the procedure to eliminate their risk of ovarian cancer. Likewise, women with a strong family history of ovarian cancer who are age 35 and over and who have completed their families may choose to have their ovaries removed to eliminate their risk of ovarian cancer.

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Myth

There is nothing I can do to prevent ovarian cancer.

Fact

There are many ways to reduce the risk of developing ovarian cancer. Anything that inhibits a woman from ovulating every month significantly reduces the risk of ovarian cancer, including use of oral contraceptive birth control pills, pregnancy (the more pregnancies, the greater the protection), and breastfeeding. Although the mechanism is unknown, *tubal ligation* (having one's fallopian tubes tied to prevent pregnancy) also significantly reduces the risk of ovarian cancer. Following a low-fat, high-fiber diet also may help.

Myth

If ovarian cancer is exposed to air at surgery, the cancer will spread rapidly.

Fact

Many people know friends or relatives who have undergone major abdominal surgery for advanced cancer whose cancer has progressed rapidly after surgery. Most believe that general anesthesia and surgery (i.e., the air) reduced the patient's immunity against the disease and resulted in rapid progression of cancer. Air, however, has no effect on cancer; although anesthesia and major ovarian cancer surgery may place stress on the immune system, these factors do not contribute to rapid progression of the cancer. Rather, the lack of response to treatment is the actual culprit.

How Is Ovarian Cancer Treated?

Ovarian cancer may be treated in several different ways.

SURGERY

Surgery is needed to treat all stages of ovarian cancer, and most patients with ovarian cancer require surgery followed by chemotherapy.

Laparotomy: Laparotomy helps the physician to make a definitive diagnosis, to determine the extent of the spread of cancer and degree of differentiation (stage and grade), and to remove all the cancer or as much as possible. Patients with very early disease (Stage I) and well- or moderately differentiated (grade 1 or grade 2) tumors will not require additional chemotherapy. Unfortunately, these characteristics occur in only a small percentage of ovarian cancer patients. Most patients have more advanced disease and require chemotherapy.

Surgical Staging: The initial surgical treatment, *laparotomy*, involves a surgical incision through the abdominal wall and into the abdominal cavity and must include complete surgical staging.

The procedure begins with a midline incision in the abdomen from the *pubis*, the bone forming the front of the pubic area at the bottom of the abdomen, to the *umbilicus* (navel). On entering the abdominal cavity, the surgeon collects any fluid in the abdomen, and then sends the fluid for microscopic examination to detect any cancer cells (*cytological examination*). If no fluid is present, the pelvis and different portions of the abdomen are flushed with sterile fluid, and the fluid then is removed and sent for a microscopic examination that is similar to a Pap test. The diaphragm is scraped with a brush, and the cells collected

on the brush are spread on a glass slide, and the slide is sent for an examination of the cells.

Cancer cells from the pelvis, the abdomen, and the diaphragm are important in determining the stage of the tumor and establishing treatment strategies. Surgical staging also involves removing the omentum and the pelvic and abdominal lymph nodes. The ovary containing the tumor should be removed and examined immediately under a microscope; this examination, called a *frozen section*, confirms the diagnosis of ovarian cancer and ensures that the cancer actually started in the ovary and did not spread to the ovary from other organs.

If the cancer is diagnosed as *metastatic* (traveling from one part of the body to another), a search for the primary tumor, such as a tumor of the large bowel, should be done. If ovarian cancer is diagnosed, both ovaries, the fallopian tubes, and the uterus should be removed. This is a *total abdominal hysterectomy with bilateral salpingo-oophorectomy*.

Debulking Surgery: Many ovarian cancer patients have cancer deposits in other parts of the pelvis or the abdomen that sometimes involve the large or small bowel. All or the largest possible amount of tumor deposits or suspicious areas in other parts of the pelvis and abdomen should be removed and sent for *pathological examination* (inspection of disease). This type of surgery has become known as *debulking surgery*, since its purpose is to remove as much of the large (bulk) tumor deposits as possible.

Several studies have shown that prognosis and survival depend on how much tumor is left at the time of initial surgery. Patients with no residual tumor or with only tumor nodules measuring less than 1 cm (3/8 inch) have the best chance for cure and long-term survival. Therefore, it is important that the initial surgery be performed by an *oncologist* (physician who deals with cancer specifically) trained to perform this type of surgery, most of whom are gynecologic oncologists. Patients with no residual tumor left or only nodules measuring less than 1 cm in

Myth

I had a total hysterectomy, which means removal of the ovaries, so I can't get ovarian cancer.

Fact

Total hysterectomy refers to the removal of the body of the uterus and the cervix; it does not refer to the removal of the ovaries. Total hysterectomy and bilateral salpingo-oophorectomy refer to removal of the uterus, tubes, and ovaries.

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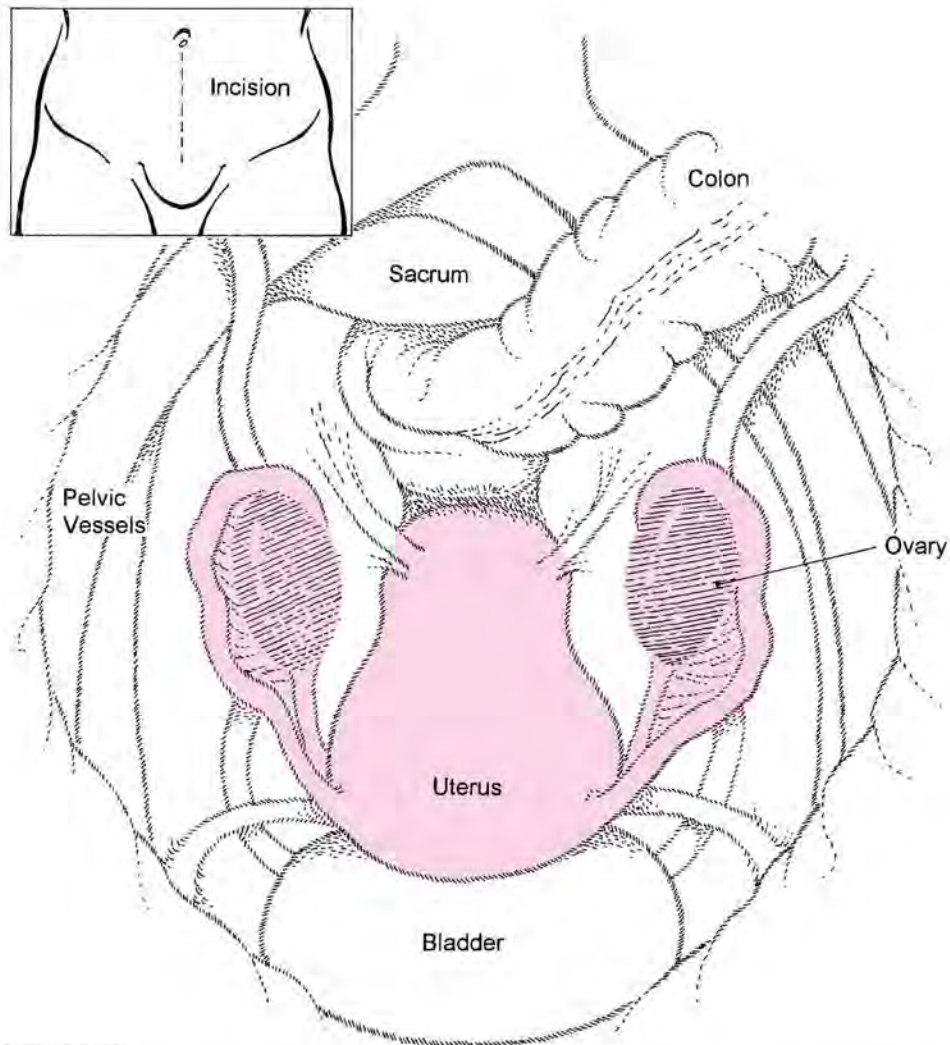


FIGURE 15

Hysterectomy – Here the artist shows the anatomy that would be removed in a hysterectomy and oophorectomy (removal of uterus and ovaries). Technically it's called a salpingo-oophorectomy.



FIGURES 16-18

Deborah Bradley Rutherford – Before and After. Even the loss of her hair cannot dim Deborah's smile! Cancer therapy may have robbed Deborah of her hair, but not of that inner glow. The Look Good...Feel Better program (see page 58) obviously taught her that beauty involves more than just hair on her head. With the right cosmetics and a very becoming wig, Deborah is ready for any occasion – and is especially looking forward to her wedding and a beautiful happy life!



Myth

Everyone gets very ill from chemotherapy.

Fact

With the recent development of new anti-nausea drugs that block receptors in the brain that bring about nausea and vomiting, 60% of women receiving platinum-based chemotherapy for ovarian cancer have little or no nausea and vomiting. This class of drugs includes ondansetron (Zofran), granisetron (Kytril), dolasetron (Anzemet), and palonosetron (Aloxi). With addition of a corticosteroid to this type of drug, 90% of women have little or no nausea and vomiting during their chemotherapy. However, these drugs are not as effective in those women who develop delayed nausea and vomiting several days after completing their chemotherapy.

diameter are said to have undergone optimal debulking surgery. Patients left with tumor nodules larger than 1 cm in diameter are said to have undergone suboptimal debulking surgery.

CHEMOTHERAPY

Chemotherapy kills cancer cells by stopping them from dividing and reproducing rapidly. Unfortunately, drugs used for chemotherapy are not absolutely specific for cancer cells and also affect normal cells that divide rapidly, such as red blood cells, white blood cells, platelets, hair cells, and cells lining the digestive tract from the mouth to the anus. Therefore, almost all chemotherapy drugs are associated with side effects.

Medications can be given before, during, and after treatment to minimize side effects such as nausea, vomiting, and diarrhea. Patients should be encouraged to increase their fluid intake to prevent dehydration. Hair loss caused by many, but not all, chemotherapy drugs is temporary.

Fortunately, ovarian cancer almost never involves the bone marrow, where red and white blood cells and platelets are produced. The body is able to replenish these important cells, usually between courses of chemotherapy, and avoid side effects caused by a drop in the number of white blood cells (infection), red blood cells (anemia, fatigue, dizziness), and platelets (bleeding). Patients have their blood checked every week or twice weekly between courses of treatment.

Different classes of chemotherapy drugs act at different points during the cell cycle of the cancer cells. For this reason, two or more different classes of chemotherapy drugs usually are given to maximize the ability of the drugs to kill cancer cells. Combining two or more chemotherapy drugs also helps prevent cancer cells from becoming resistant to the individual drugs.

Different chemotherapy regimens are given depending on the patient's condition, the type of ovarian cancer she has, and her response to previous

chemotherapy. For example, patients who have kidney disease are not usually given chemotherapeutic agents that can adversely affect the kidney.

Most chemotherapeutic agents are given *intravenously* (through a vein) in a cycle every 3-4 weeks. Some patients whose veins are not suitable to accept drugs have an indwelling venous *catheter* (flexible tube) inserted in a neck or chest vein to make treatment easier; drugs can then be given through this tube instead of piercing the skin repeatedly with a needle. The part of the catheter that the needle is inserted into for injection of the drug can be implanted into the skin (Mediport) or can remain external (Groshong).

Many chemotherapy regimens are given on an outpatient basis; others are given over several days and require that the patient remain in the hospital. Specially trained nurses help administer the chemotherapy, watch for side effects, and follow patients between cycles.

First-Line Chemotherapy: Most patients with ovarian cancer require postoperative chemotherapy, usually with paclitaxel (Taxol) and carboplatin (Paraplatin) or cisplatin (Platinol), the most effective combination of drugs. This is referred to as *first-line chemotherapy*. Most patients receiving first-line chemotherapy for ovarian cancer are able to enjoy an excellent quality of life. Clinical studies on the effectiveness of the newer drugs as first-line chemotherapy for ovarian cancer are underway.

Monitoring First-Line Chemotherapy: Ovarian cancer patients usually are scheduled to receive six courses of chemotherapy, provided that they show clinical evidence of complete response. The response to chemotherapy is assessed before each treatment by physical examination, measuring blood levels of the tumor marker CA125, and if indicated, a CAT scan. Patients whose CA125 level falls below the normal value of 35 U/mL before their third course of treatment have the best chance of *remission* (clearing up of a disease).

Myth

The stage of my ovarian cancer doesn't matter, since all ovarian cancer requires chemotherapy.

Fact

Most cases of Stage I ovarian cancer do not require chemotherapy and have a long-term cure rate of over 95% with treatment limited to surgery.

*Life is a gift –
appreciate
each day.
Experience it!*

I had friends and relatives who had cancer years ago. They got horribly sick during treatment. I was surprised how things have changed. I'm worried about gaining weight.

Second-Line Chemotherapy: Although 70% to 80% of women will achieve a complete remission with first-line chemotherapy (defined as a normal CA125 blood level, a negative CAT scan of the pelvis and abdomen, and a negative physical examination), the majority will develop a recurrence of their ovarian cancer at some time in the future. Many patients may be re-treated with the same drugs they received as first-line chemotherapy, or they may receive one of the many effective second-line agents against ovarian cancer. In such a setting, controlling the cancer for long periods of time, while maintaining good quality of life, becomes a major goal. Topotecan (Hycamtin) is effective as second-line chemotherapy with minimal cumulative side effects with prolonged treatment. Other effective second-line drugs include gemcitabine (Gemzar), liposomal doxorubicin (Doxil), etoposide (VePesid), hexamethylmelamine (Hexalen), and docetaxel (Taxotere). See page 46 for more on "What Happens if Ovarian Cancer Recurs?"



FIGURES 19-21

Roberta Tyner – Before and After. Losing your hair is really a small price to pay for regaining your life. Life-saving chemotherapy can result in alopecia, or hair loss, of the head and eyebrows. In most cases, hair does grow back. Meanwhile, skillful application of make-up, an attractive wig, and a good attitude can bring inner beauty outward, as Roberta shows here.

Second-Look Surgery: Patients who show a clinical response to chemotherapy, whose CA125 levels decrease to normal, and whose signs of ovarian cancer completely disappear based on physical examination and CAT scan are sometimes offered second-look surgery. This surgical procedure is done at the end of chemotherapy in responsive patients to check tissue under the microscope once again. Second-look surgery can be performed by laparotomy or laparoscopy.

During second-look surgery and abdominal wash, biopsies are obtained from any suspicious looking nodules and from areas where cancer was known to have been, and cells again are gathered from fluid washed over these areas. About 50% of patients whose levels of CA125 are within normal limits and who show no evidence of cancer on physical examination and CAT scan will have evidence of persistent ovarian cancer at second-look surgery.



Myth

If first-line chemotherapy doesn't work, there is no hope for controlling my cancer.

Fact

Although paclitaxel and carboplatin have become standard first-line chemotherapy in advanced ovarian cancer, there are methods for controlling ovarian cancer if this combination is not effective. Examples include the use of chemotherapy delivered *intraperitoneally* (into the abdominal cavity), the newer drugs topotecan (Hycamtin), gemcitabine (Gemzar), liposomal doxorubicin (Doxil), and other drugs.

Myth

No one is ever cured of ovarian cancer.

Fact

Actually, the average survival for women with advanced stage ovarian cancer in the last 15 years has gone from 1 year to over 3 years. It is true that among women followed for 5 and 10 years after treatment, the number that are actually cured of the disease is very small. However, it appears that some 8% to 15% of patients, even those with very advanced ovarian cancer, eventually will be cured of the disease.

Chemotherapy is stopped for patients whose biopsies and abdominal wash show no cancer cells. Patients with evidence of cancer on second-look surgery should be continued on the same chemotherapy or on a different combination of drugs, depending on their level of response. *Second-line chemotherapy* refers to drugs given after failure of first-line chemotherapy.

Topotecan is one of the newest drugs that has demonstrated effectiveness as second-line chemotherapy in ovarian cancer.

Intraperitoneal Chemotherapy: Intraperitoneal chemotherapy delivers large doses of chemotherapy drugs directly to where the tumor is located through an *intraperitoneal catheter*, a flexible tube inserted into the abdominal cavity. The drugs reach the tumor through direct contact and through the bloodstream. Only a small amount of drug is absorbed by the blood, and, therefore, side effects are reduced. Medications can be given intravenously to counteract any significant side effects. This mode of administration is only useful if the tumor nodules are small (5 mm or less), if the lymph nodes are not involved, and if there are no significant *adhesions* (abnormal bands that bind organs to one another) in the peritoneal cavity.

High-Dose Chemotherapy/Autologous Bone Marrow Transplantation: This is a new treatment for ovarian cancer that is still being evaluated. Chemotherapy drugs used share the common side effect of decreasing the blood cells. When given in high doses to increase the effectiveness of these drugs on cancer cells, these drugs also reduce the blood cells to dangerous levels.

Autologous bone marrow is bone marrow obtained from the patient being treated before her chemotherapy is started. A bone marrow transplant and an infusion of blood cells also collected from the patient before chemotherapy counteract the effects of drugs on the blood cells. Early results from this treatment indicate that it has a high response rate. However, there presently is no indication that it leads to prolonged survival in ovarian cancer patients.

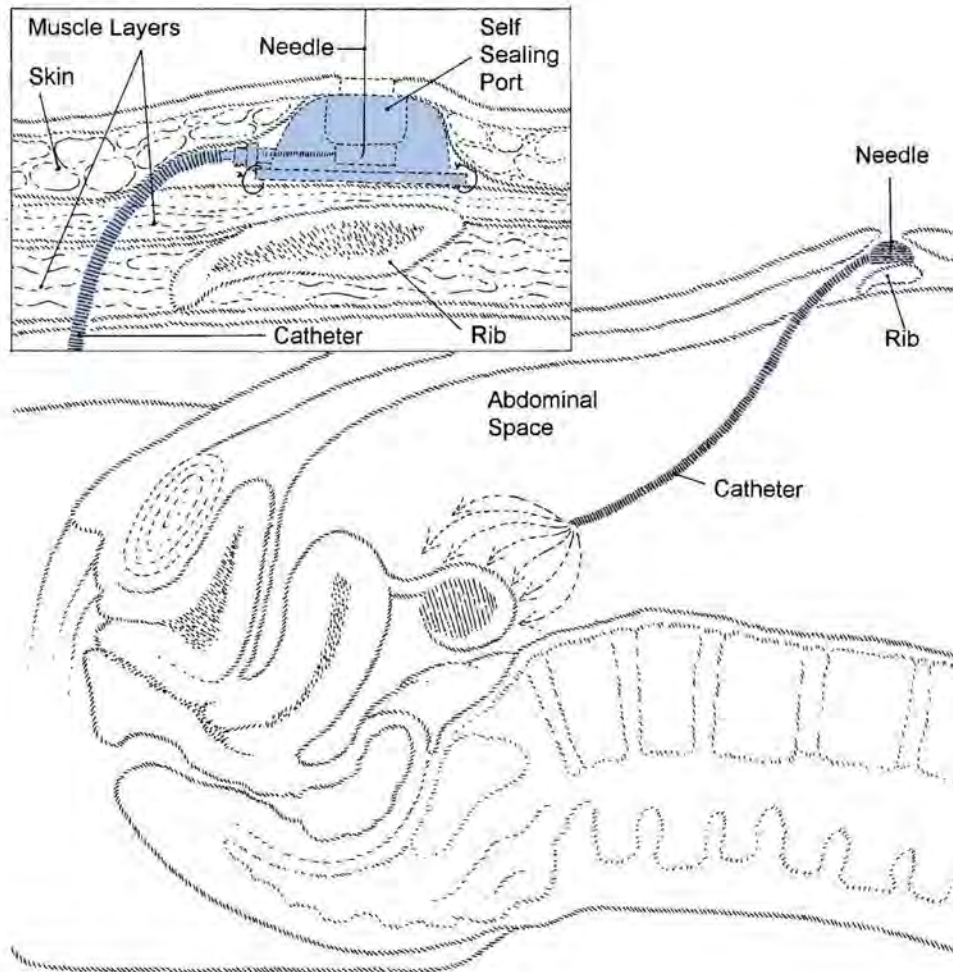


FIGURE 22

Intraperitoneal Chemotherapy – How chemotherapy is administered directly into the abdominal and pelvic cavity. The diagram shows an intraperitoneal catheter that is used to deliver high doses of chemotherapy drugs to the peritoneal cavity, where ovarian cancer usually spreads. This form of treatment is especially effective against small tumor metastases. To help you orient yourself to the anatomy, the ovaries are shown in place. In actuality, by the time a woman would be receiving intraperitoneal chemotherapy, the ovaries would have already been removed via surgery.

*Losing your hair
is the worst! I felt
like I lost all my
femininity – you
stand in front of the
mirror and you
look like a little girl.*

RADIATION THERAPY

Radiation therapy has a limited role in treating ovarian cancer. Because ovarian cancer cells spread widely within the peritoneal cavity, effective radiation therapy requires treatment of the entire area. Abdominal organs such as the small bowel, liver, and kidneys cannot tolerate the doses of radiation needed to kill cancer cells. Significant side effects (abdominal cramps, diarrhea, and bowel obstruction) can also occur. However, when ovarian cancer is limited to the pelvis with no evidence of spread to the abdomen, radiation therapy can be given effectively with tolerable side effects.

An effective way of delivering radiation therapy to the whole abdomen is by injecting a radioactive chemical (e.g., chromic phosphate [P32]) into the peritoneal cavity. This treatment might be valuable in some patients with ovarian cancer limited to one or both ovaries if the cyst ruptures during surgical removal or if there is no evidence of spread to other abdominal organs or pelvic lymph nodes. It also could be used in certain patients who have either no evidence of cancer or only microscopic disease at second-look surgery. Side effects of radiation therapy include abdominal pain, inflammation and irritation of the peritoneal lining, adhesion formation, and small bowel obstruction. The treatment is not appropriate if significant intraperitoneal adhesions are found.

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What Is Gene Therapy?

Gene therapy offers both a powerful new weapon for physicians to treat ovarian cancer and new hope for women with this disease.

Ovarian cancer results from cumulative changes in the genes of the cells that make up the ovary. Some of these defects can be inherited. Most genetic defects in ovarian cancer occur after the patient is exposed to an environmental factor or some other event that effects cells of the ovary.

Given that ovarian cancer is essentially a disease caused by gene defects, can these gene defects be repaired? And, if so, will this repair result in a cure for women with ovarian cancer?

Advances in genetic engineering have given researchers the tools to hopefully correct or change a woman's chances of developing cancer because she has a family history of the disease; this may be accomplished by transplanting normal copies of genes into cells that have defective genes. These tools may also make it possible to deliver chemotherapy directly to the tumor and to make tumors more sensitive to chemotherapy and less likely to become resistant to therapy.

Gene therapy has been shown to be possible in theory and is exciting to think about, but its practical applications and implications for cure are still evolving. More than 100 clinical trials have been designed to evaluate the safety, side effects, and clinical benefits of gene therapy.

Results of these early studies are not available. Clearly, the final verdict on gene therapy for ovarian and other cancers is probably years away.



*I always tell people
“don’t wait to get
sick to smell the
roses. Tell someone
you love them, spoil
yourself, drink in
nature, enjoy life!”*

*“Please, someone,
protect me from
this cancer. Make
me feel safe again.”*

— Gilda Radner, in
It's Always Something

*Many men
have said to me,
'I don't know if
I can handle this...
honestly, I just
don't know,' as if
they were the ones
who had ovarian
cancer. But if they
only knew how the
littlest thing can
boost the morale of
their partner, who
might very well be
living in a sweating
panic, day and
night, afraid to
admit how truly
frightened she is
and how much she
might long for
something normal
in her life, some-
thing as simple as
an argument.*

How Are Ovarian Cancer Patients Followed After Treatment?

Patients whose ovarian cancer goes into remission following treatment need continuing follow-up by experienced physicians. Regrettably, many patients who respond to chemotherapy and have no evidence of persistent ovarian cancer at second-look surgery are likely to have a recurrence of their cancer. Early ovarian cancer recurrence usually produces no symptoms. Therefore, the goal of follow-up care is to detect recurrence as early as possible and begin treatment when it is likely to be more effective.

Follow-Up Examinations: The physician and the patient together should determine the frequency of follow-up visits. Usually, however, patients who have had negative second-look surgery are examined every 3 months for the first 2 years; these visits are usually repeated every 4 to 6 months thereafter. Patients should report anything that could indicate recurrence to their physicians, including change in appetite, nausea, vomiting, change in bowel habits, and weight gain or loss.

At each follow-up visit, the physician should review the patient's history, check for any new symptom, and perform complete general physical, abdominal, and pelvic examinations. Above all, it is critically important that the physician check the patient's serum CA125 level. Although there are exceptions, recurrence of ovarian cancer can be detected in patients who had elevated serum CA125 levels when ovarian cancer was first diagnosed, experienced normal levels after treatment,

and then have increased CA125 levels again. In these patients, CAT scans should be performed to find the site of recurrence. A negative CAT scan does not rule out that the cancer has recurred, however, because only masses larger than 1-2 cm can be seen using this test. Therefore, in patients whose serum CA125 levels are elevated once more and CAT scan results are negative, a biopsy or microscopic examination of peritoneal cells should be done to confirm the diagnosis of recurrent cancer.

Secondary Debulking Surgery/Chemotherapy:

Patients who have recurrence of ovarian cancer might undergo secondary debulking surgery; however, the medical benefits of this practice remain controversial. In addition to confirming the diagnosis of recurrence, the goal of this surgery is to remove as much cancerous tissue as possible, which, in turn, may give more chemotherapy a higher chance of success.

Patients who do not have secondary debulking surgery are treated with chemotherapy. In both groups, the type of chemotherapy used depends on the type of chemotherapy used previously and how the patient responded to this chemotherapy.

Hormone Replacement Therapy: The use of hormone replacement therapy in patients treated for ovarian cancer also is controversial. The value of hormone replacement therapy is well established in decreasing the chance of osteoporosis and in relieving hot flashes in menopausal patients or in younger patients who have had their ovaries removed. While some physicians think that the use of estrogen might increase the chances of cancer recurrence, there is no scientific proof that this is true. On the other hand, there is no scientific proof that the use of estrogens in these patients is safe.

The decision to use hormone replacement therapy should be made by the physician and patient after a thorough discussion of the risks and benefits involved.

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“When I finally had the courage to shout at Gilda because I was fed up to the bursting point over some unjust act of hers, Gilda started crying, ‘Thank you, thank you, honey. I know you would not argue with me if you thought I was dying. See?...it’s good to have a fight. It is nice! Now I feel normal again.’”

— Gene Wilder in:
Gilda’s Disease:
Sharing Personal
Experiences and a
Medical Perspective on
Ovarian Cancer

Myth

Ovarian cancer is a terminal illness and there is little hope for women diagnosed with advanced disease.

Fact

Advances in therapy and improvements in understanding how and when to deliver which treatment have enabled oncologists to treat ovarian cancer like a chronic disease in some women. By careful and knowledgeable selection of which treatment is most appropriate for an individual, recurrent ovarian cancer can be treated. Cure may not be the goal of treatment, though it is possible to extend survival and preserve a good quality of life during treatment.

What Happens If Ovarian Cancer Recurs?

The majority of patients with ovarian cancer are diagnosed when the disease is at a more advanced stage, and so many of these women may experience one to several recurrences of their illness following initial treatment. Due to improvements in diagnostic tools and a wider availability of effective chemotherapeutic options in recent years, management of recurrent ovarian cancer is possible. And in some patients, recurrent ovarian cancer can be treated as a chronic illness, with chemotherapeutic options that afford patients the opportunity to live longer lives, while maintaining a good quality of life.

TREATMENT OF RELAPSED OVARIAN CANCER

Several factors will affect what options are available for treatment of recurrent disease, including a patient's response to her initial therapy and the duration of that response. In women whose ovarian cancer has recurred 6 months or more after completion of initial therapy, the same chemotherapy regimen used initially, often a platinum-containing compound such as carboplatin and a taxane such as paclitaxel, may be used again. Single-agent therapy may be another option. A patient's chance of responding to subsequent treatment with the same chemotherapy regimen she received initially is considered good in such cases because response to initial therapy lasted for 6 months or more.

If a recurrence of ovarian cancer occurs less than 6 months after completion of initial therapy, a change to different chemotherapeutic drugs may be an option, and is often the preferred treatment. The very short response time is strongly suggestive that the cancer is truly resistant to the initial drugs.

OPTIONS IN TREATMENT OF RECURRENCE

In addition to platinum and taxane agents, several drugs have proven to be effective in treating recurrent ovarian cancer, including topotecan (Hycamtin), liposomal doxorubicin (Doxil), etoposide (VePesid), and gemcitabine (Gemzar). Some of these drugs may be better tolerated than others, though still effective in treating recurrent disease.

With these newer effective chemotherapy drugs, recurrent ovarian cancer can be treated like a chronic disease in some women, who may experience periods of treatment for recurrence followed by periods of remission in which they are symptom-free. The order in which a particular chemotherapy combination or single agent is given for treating a first, second, or later recurrence is important. Patients are advised to speak with their physicians about which therapy may be most effective for treating their recurrent disease, and in what order a particular therapy should be given to achieve the best response to treatment.

Factors to consider in determining which chemotherapeutic option may be most appropriate for recurrent disease include not only how well a patient responded to her initial treatment, as well as how long that response lasted, but can include preventing the cancer from progressing, in other words, maintaining stable disease, and minimizing chemotherapy side effects, along with preserving a good quality of life during treatment.

Patients are encouraged to communicate with their oncologists, physicians, and health care team about their own treatment goals and their own experiences with side effects and response to therapy. Communication is key to a better understanding of ovarian cancer and options that are available for treatment of recurrent disease.

While research continues to find more effective and possible curative agents against ovarian cancer, drugs such as topotecan, liposomal doxorubicin, etoposide, and gemcitabine offer women being treated in the 21st century for recurrent ovarian cancer the realization that there is indeed active therapy for their disease.

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*It's hard to
convince your
family and friends
that you are the
same person as you
were before your
cancer diagnosis.
I want to live my
life. Life is a
process I want to
continue.*

How Does a Patient Cope With Ovarian Cancer?

Myth

Sexual relations should be avoided because ovarian cancer is contagious.

Fact

Ovarian cancer is not contagious and cannot be transmitted by sexual intercourse or any other form of intimacy.

Women experience very strong, devastating emotional reactions when they are diagnosed with ovarian cancer. Even the mention of this disease brings on thoughts of loneliness, disfigurement, disabling treatment, and eventual death. Anxiety, panic, and depression are common psychological reactions. The patient's self-esteem and sex life and her interactions with her partner, family, and co-workers also may be greatly changed by ovarian cancer. It is important that the medical team, the patient's family and friends rally around the patient to form a mutual support network that enables the patient to begin treatment with a positive and hopeful outlook.

Psychological/Spiritual Support: The first step in coping with ovarian cancer is to recognize that it now is part of this woman's life. She can seek support from family, friends, and outside sources to help her cope with the difficult periods of diagnosis and treatment and may find the greatest support within herself and/or her religious beliefs.

Ovarian cancer patients are not fighting ovarian cancer alone. They always can depend on the support of their physicians, nurses, nurses' aides, and social workers. As patients share the diagnosis with family and co-workers and accept their support, coping with the disease and the treatment that follows becomes easier.

Patients diagnosed with any type of cancer often feel guilty. In women diagnosed with ovarian cancer, this feeling may be more intense due to the genetic impact the disease can have on their daughters. Patients should

be helped to understand that the cancer is not their fault; *they did nothing to bring on the disease, and could do nothing to prevent it.* The cancer is now a fact of life that has to be dealt with in the present; nothing in the past can be of any help, and looking positively to the future is the best bet.

Many women find comfort, assurance, and help from support groups. These groups are usually formed by women with ovarian cancer who are undergoing treatment and who have survived the disease. Sharing concerns, knowledge, and experiences with other women who *know* what others are going through *firsthand* may be helpful. Information about support groups in a particular community can be obtained from the patient's medical team and from specialized organizations (see Appendix 1).

Sexual Aids/Counseling: Diagnosis and treatment of ovarian cancer may have a significant impact on a woman's sexual life. It is not uncommon for men and women to lose interest in sex during treatment for cancer, at least for a time.

Frequently, women with ovarian cancer may experience pain during intercourse because the vagina was shortened during hysterectomy; some patients experience vaginal dryness from lack of estrogen after the ovaries are removed. Some chemotherapy drugs irritate all of the body's mucous membranes, including the vagina; vaginal yeast infections also are common during chemotherapy. Any one of these can make intercourse painful.

If a woman needs extra lubrication to make intercourse comfortable, a vaginal lubricant such as K-Y Jelly, Surgilube, or Replens, often is helpful. Almost all women who could achieve orgasm before they had cancer should be able to achieve it after treatment.

Women taking chemotherapy often have less desire for intercourse. Side effects of chemotherapy, such as nausea and vomiting, may leave little energy for intimate relationships. Women taking chemotherapy also may feel unattractive because of hair loss and other reactions that interfere with their sexual self-image.

The first step in finding help for a sexual problem is discussing it with a physician or nurse. These professionals can help in resolving the problem or suggest

*If you have cancer,
you better have a
sense of humor –
sometimes that's
the only thing
that helps!*

Myth

Sexual relations should be avoided because ovarian cancer will get worse or recur.

Fact

From a scientific point of view, there is no reason for sexual relations to make ovarian cancer worse or to cause the cancer to return.

a specialist in sexual problems. Most couples find that by talking about their sexual problems, their sexual life after cancer can be as enjoyable and as fulfilling as it was before cancer came into their lives.

Sexual sharing is one way for a couple to feel close during the stress of an illness. Ovarian cancer patients and their partners should learn about the effect the disease has on sexual desire and relationships and what to expect when resuming sexual activity. Patients should learn to focus on their positive features and to combat negative thoughts. Good communication between the patient and her partner is the most important part of resuming sexual activity.



FIGURE 23

The Gilda Radner Familial Ovarian Cancer Registry –
This photo shows the entrance and one of the staff of the Gilda Radner Familial Ovarian Cancer Registry at Roswell Park Cancer Institute. As part of its comprehensive care of women with ovarian cancer, the registry keeps track of women in families with two or more first degree relatives (mother and daughter, two sisters) who have or had ovarian cancer. The registry was founded by Dr. Piver and Gene Wilder, Gilda Radner's husband, after Ms. Radner died of ovarian cancer.

2

Glossary

Abdomen: The part of the body below the diaphragm between the chest and the pelvis that contains organs such as the liver, the bowel, the bladder, the kidneys, the ovaries and the uterus.

Alopecia: Loss of hair.

Aneuploid: Cells that contain an abnormal number of chromosomes.

Anemia: A deficiency of red blood cells.

Antibody: A substance produced by the body to defend the body against infection.

Antiemetic: A medication given to prevent nausea and vomiting.

Antigen: A foreign substance in the body, such as protein, bacteria, viruses, or other materials, that stimulate the body to produce antibodies against them.

Ascites: An accumulation of fluid within the abdomen that can occur in women with noncancerous conditions (e.g., liver cirrhosis) and with different types of cancer.

Autologous Transplant: Tissue taken from a patient and returned to the same patient.

Benign: Noncancerous.

Biopsy: Microscopic examination of tissues and cells removed from the body to determine the presence of cancer.

CA125: A blood protein that can be measured and is an important tumor marker in ovarian cancer.

Cancer: A general term for more than 100 diseases characterized by uncontrolled, abnormal growth of cells in different parts of the body that can spread to other parts of the body.

Carcinogens: Substances known to cause and/or to promote cancer.

Carcinoma: One of the basic types of cancer in which the cancerous tumor begins in the tissues that line the skin and mucous membrane in the glands, lung, ovary, etc.

Cell: The basic structure of living tissues; all plants and animals are made of one or more cells.

Chemotherapy: Treatment or control of cancer using anticancer drugs that destroy cancer cells by interfering with their growth and/or preventing their reproduction.

Colonoscopy: A procedure used to examine the interior of the colon (the lowest part of the large intestine).

Colostomy: A surgical procedure performed to create a new opening in the body wall for the elimination of waste.

Combination Chemotherapy: More than one (generally between 2 and 4) different anticancer drugs used together to treat cancer.

Complete Blood Count: A test to check the number of red cells, white cells, and platelets in a sample of blood.

CT or CAT Scan (Computerized Axial Tomography): A diagnostic procedure that combines an x-ray with a computer to produce highly-detailed, cross-sectional, three-dimensional pictures of the entire body. These tests are generally 100 times more sensitive than x-rays.

Cyst: A fluid-filled sac.

Cystoscopy: A visual examination of the interior of the bladder using a lighted, tubular instrument (a cystoscope).

Cytotoxic Drug: A drug that kills specific cells in the body.

Diagnosis: The procedure by which a disease is identified.

Diploid: Cells that contain a normal number of chromosomes.

Drug Resistance: A condition in which a person's cancer cells no longer respond to chemotherapy.

Enteral Feeding: A method of providing nutritional support to malnourished patients through tubes, e.g., a nasogastric tube or gastrostomy tube.

Epithelial: Type of tissue lining the skin and hollow organs.

Estrogen: Female sex hormone secreted primarily by the ovaries that is responsible for secondary sex characteristics, such as the growth of breasts.

Estrogen Receptor Test: A test done during the biopsy of cancerous tissue to determine if its growth depends on estrogen.

Flow Cytometry: A procedure that measures the amount of DNA in cells.

Gastrostomy Tube: A surgical procedure is performed to create an opening in the stomach, which is usually connected to the skin of the abdomen with a tube.

Gene: The biologic unit of heredity that determines the traits a person gets from past generations.

Hickman Catheter: A hollow silicone tube inserted and secured into a large vein in the chest for long-term administration of drugs or nutrients.

Hospice: Program for caring for terminally-ill patients with less than 6 months life expectancy which focuses on improving the quality of life for whatever time the patient has left.

Hysterectomy: Surgical removal of the uterus.

Ileostomy: A surgical procedure performed to create an opening in the ileum (the lower part of the small intestine) for the elimination of digestive wastes when the colon is removed.

Infuse-a-Port (Mediport): A small device containing a thin catheter that is generally implanted under the skin for administration of drugs and nutrients.

Invasive: Growing into and destroying normal tissues.

Laparoscopy: Examination of abdominal organs with a laparoscope (a lighted tubular instrument) passed through a small incision in the abdominal wall.

Laparotomy: Any surgical procedure which involves opening the abdominal cavity for examination (exploratory laparotomy) or to perform additional surgery.

Lymph Nodes: Small glands located throughout the body that filter out and destroy bacteria and that can collect cancer cells.

Lymphadenectomy: Surgical removal and biopsy of lymph nodes to determine the spread of cancer.

Malignant: Cancerous.

Menopause: The time in a woman's life when the ovaries stop producing estrogen and the woman stops having periods.

Metastasis: The spread of cancer from one part of the body to another.

MRI (Magnetic Resonance Imaging): A new, sophisticated technique to examine the body using powerful electromagnets, radiofrequency waves, and a computer to produce internal pictures of the body.

Nasogastric Tube: A catheter inserted into the stomach through the nose and throat.

Oncogene: A heredity unit that controls the growth of cancer cells.

Oncologist: A doctor who specializes in the diagnosis and treatment of cancer.

Oophorectomy: Surgical removal of one (unilateral) or both (bilateral) diseased ovaries.

Pap (Papanicolaou) Smear: The microscopic examination of cells from the vagina or the cervix of the uterus.

Paracentesis: Removal of fluid from the abdominal cavity, the space between the abdominal wall and organs.

Peritoneum: A transparent membrane that lines the inside of the abdomen.

Prognosis: A prediction about the possible outcome of a disease.

Pleural Effusion: An accumulation of fluid within the pleural cavity, the space between the lungs and the interior walls of the chest.

Radioactive: Emitting energy in the form of waves or particles.

Recurrence: Reappearance of a cancer.

Remission: The decrease or disappearance of disease.

Sigmoidoscopy: An examination of the first 10-12 inches of the rectum with a sigmoidoscope (a thin, lighted metal or plastic tube) inserted through the rectum.

Staging: A method to describe the extent of cancer, using such characteristics as the size of the tumor, lymph node involvement, and where it has spread.

Thoracentesis: Removal of fluid from the chest cavity, the space between the lungs and the chest wall.

Thrombocytopenia: A drop in the number of platelets, the blood cells responsible for clotting.

Total Parenteral Nutrition (TPN): Providing nutrients to a malnourished patient via a large vein.

Tumor: An abnormal growth of cells that can be benign or malignant.

Ultrasound (Ultrasonography, Sonogram): An examination to locate and measure cystic tumors using very high frequency sound waves, which the human ear cannot hear.

Vaccine: A substance that contains part of the antigen from an infectious agent. It protects against infection from that organism in the future by stimulating the immune response to it.

Virilism: Masculinizing condition occurring in women, which may include infrequent menstrual periods, cessation of menstrual periods before menopause, hoarse voice, and appearance of facial hair.

White Blood Cells: The blood cells responsible for fighting infection.

X-Ray: High-energy electromagnetic waves of very short length that can penetrate the body and produce pictures.

❧

APPENDIX I

Resources for Ovarian Cancer Patients

American Cancer Society (ACS)
(800) ACS-2345
www.cancer.org
1599 Clifton Road, NE
Atlanta, GA 30329-4251

The American Cancer Society is a nationwide, community-based, voluntary health organization dedicated to eliminating cancer as a major health problem. The ACS has materials in Spanish and Chinese.

American College of Medical Genetics
(301) 634-7127
www.acmg.net
9650 Rockville Pike
Bethesda, MD 20814-3998

Their website includes “Genetic Susceptibility to Breast and Ovarian Cancer: Assessment, Counseling and Testing Guidelines” (produced in collaboration with the NYS Department of Health). The guidelines are also available on the NYS Department of Health website at www.health.state.ny.us (click on Information for Providers/Clinical Guidelines).

American College of Obstetricians and Gynecologists Resource Center
(202) 638-5577
www.acog.org
409 12th Street SW
PO Box 96920
Washington, DC 20090-6920

American College of Obstetricians and Gynecologists Resource Center is a professional organization of physicians who specialize in women’s health care.

American Medical Association (AMA)
(800) 621-8335
515 North State Street
Chicago, IL 60610

The American Medical Association provides information on doctors, such as when they were licensed, their specialty, and board certification. The Directory of Medical Specialists lists qualifications of medical doctors and should be available in medical libraries and the public library.

American Society of Clinical Oncology (ASCO)
(703) 299-0150
www.asco.org
1900 Duke Street, Suite 200
Alexandria, VA 22314

ASCO can provide referrals to gynecologic oncologists in your area.

Cancer Care, Inc.
(800) 813-HOPE (Long Island); (212) 712-8080 (New York City)
www.cancercare.org
275 Seventh Avenue, Floor 22
New York, NY 10001

Cancer Care, Inc., is a national nonprofit agency dedicated to providing emotional support, information, referral, and practical assistance to people with cancer and their loved ones at no charge.

Cancer Information Service
(800) 4-CANCER or (800) 422-6237
(800) 332-8615 (TTY for deaf and hard-of-hearing callers)
9:00 AM–4:30 PM, Monday through Friday
www.cis.nci.nih.gov

The Cancer Information Service is a national information and education network sponsored by the National Cancer Institute. Information is available in English and Spanish.

Cancer Risk Assessment Survey
Women's Cancer Network
www.wcn.org

The Cancer Risk Assessment Survey is an online, interactive cancer risk assessment survey that helps identify risk level for the gynecologic cancers.

CanSurmount
(800) ACS-2345

CanSurmount, an ACS program, provides short-term visitor programs for cancer patients and family members in the hospital and/or at the home for support and encouragement.

Centers for Disease Control and Prevention
Division of Cancer Prevention & Control
(800) CDC-INFO or (800) 232-4636
www.cdc.gov/cancer
4770 Buford Highway NE, MS K-64
Atlanta, GA 30341-3717

Continental Care Force
(281) 261-6626

Provides free air transportation to medical patients with financial need.

Conversations! The Newsletter for Those Fighting Ovarian Cancer

(806) 355-2565

www.ovarian-news.com

PO Box 7948

Amarillo, TX 79114-7948

This monthly newsletter, written by an ovarian cancer survivor, reports on treatment options, trials, coping skills, and early-detection strategies. *Conversations!* offers humor and an upbeat tone. A networking service to match women in similar circumstances is available.

Coping With Cancer Magazine

(615) 790-2400

PO Box 682268

Franklin, TN 37068-2268

This is a bimonthly magazine for people who have been touched by cancer. Issues include patient education articles by health-care professionals.

Corporate Angel Network

(914) 328-1313

www.corpangelnetwork.org

1 Loop Road

White Plains, NY 10604-1215

Corporate Angel Network is a nonprofit organization that finds space on corporate jets for cancer patients and one attendant/family member needing transportation for treatment, consultation, and checkups at no charge to the patient.

Department of Defense Ovarian Cancer Research Program

(Congressionally Directed Medical Research Program)

(301) 619-7071

<http://cdmrp.army.mil/>

FORCE (Facing Our Risk of Cancer Empowered, Inc)

(954) 255-8732

www.facingourrisk.org

16057 Tampa Palms Blvd W, PMB #373

Tampa, FL 33647

This is an organization for those at increased risk of breast/ovarian cancer due to positive family history and/or BRCA mutations. Patients can gather information and support, communicate with others, learn through librarian-selected links, and locate specialists.

Gilda Radner Ovarian Cancer Familial Registry

(800) OVARIAN

www.ovariancancer.com

Roswell Park Institute

Elm and Carlton Streets

Buffalo, NY 14263

The Registry tracks families with a history of ovarian cancer, and offers a help-line, education, information, and peer support for women with high risk (family history) of ovarian cancer.

Gilda's Club Worldwide

(888) GILDA-4-U
www.gildasclub.org
322 Eighth Avenue, Suite 1402
New York, NY 10001

Gilda's Club provides a place where people living with cancer, their families, and friends can join others to build social and emotional support as a supplement to medical care.

Gynecologic Cancer Foundation (GCF)

(800) 444-4441
info@thegcf.org
230 W. Monroe, Suite 2528
Chicago, IL 60606

The GCF is a not-for-profit fundraising organization established by the Society of Gynecologic Oncologists (SGO) to support ovarian cancer research, the training of cancer specialists in laboratory research, and a variety of programs for patient education and public awareness of gynecologic cancers. Callers will be able to obtain a list of nearby specialists in gynecologic oncology, a nationwide directory of all SGO members, and informational literature.

Hereditary Cancer Institute

(402) 280-2942
Henry Lynch, MD
Creighton University School of Medicine
2500 California Plaza
Omaha, NE 68178

The Hereditary Cancer Institute provides free cancer-risk information and other forms of genetic counseling.

Lance Armstrong Foundation

(512) 236-8820
PO Box 161150
Austin, TX 78716-1150

The Foundation focuses on cancer survivorship issues for people living with, through, and beyond cancer.

Look Good...Feel Better

(800) 395-LOOK
www.lookgoodfeelbetter.org
CTFA Foundation
1101 17th Street NW
Washington, DC 20036

Co-sponsored by the Cosmetic, Toiletry and Fragrance Association, the American Cancer Society, and the National Cosmetology Association, this public service program teaches women ways to cope with appearance-related side effects of cancer treatment.

Marsha Rivkin Ovarian Cancer Research Center

(800) 328-1124
www.marsharivkin.org
1221 Madison Street, Suite 1401
Seattle, WA 98104

The Marsha Rivkin Ovarian Cancer Research Center promotes prevention, research, detection, and awareness.

National Cancer Institute (NCI)
(800) 4-CANCER
www.cancernet.nci.nih.gov

The NCI provides a nationwide telephone service for cancer patients and their families and friends, the public, and health-care professionals that answers questions and sends booklets and information about cancer.

National Coalition for Cancer Survivorship
(888) 937-6227
www.cansearch.org
1010 Wayne Avenue
Silver Spring, MD 20910

The NCCS raises awareness of cancer survivorship through its publications, quarterly newsletters, education to eliminate the stigma of cancer, and advocacy for insurance, employment, and legal rights for people with cancer.

National Hospice and Palliative Care Organization
(301) 650-9127
www.nhpco.org
1700 Diagonal Road, Suite 625
Alexandria, VA 22314

The National Hospice Organization is an association of groups that provide hospice care. Founded in 1978 to promote and maintain quality hospice care and encourage support for patients and family members, this organization can provide information on local hospices.

National Ovarian Cancer Coalition (NOCC)
(888) OVARIAN
www.ovarian.org
500 NE Spanish River Blvd., Suite 8
Boca Raton, FL 33431

The NOCC raises awareness about ovarian cancer and promotes education about ovarian cancer throughout the general population and the medical community. The NOCC has chapters throughout the country.

The Newsletter of the Gilda Radner Familial Ovarian Cancer Registry
(800) OVARIAN
www.ovariancancer.com
Roswell Park Cancer Institute
Elm and Carlton Streets
Buffalo, NY 14263-0001

NYS Ovarian Cancer Information Program
(518) 474-1222
kxg03@health.state.ny.us
NYS Department of Health
Bureau of Chronic Disease Services
Riverview Center
150 Broadway, 3rd Floor West
Albany, NY 12204

This program promotes a public health approach to ovarian cancer awareness and education.

Office of Women's Health
Department of Health and Human Services
(800) 994-9662
www.4woman.gov

Oncolink: The University of Pennsylvania Cancer Center Online Resource
www.oncolink.com

Oncolink is a comprehensive information source, including links to online discussion groups.

Ovarian Cancer National Alliance
(202) 331-1332
www.ovariancancer.org
910 17th Street NW, Suite 1190
Washington, DC 20006

The Ovarian Cancer National Alliance is a national umbrella organization that works to increase public and professional understanding of ovarian cancer, and to advocate for more effective diagnostics, treatments, and cure. Members include survivors and family members, local and national organizations, and health-care providers. Materials include awareness information and national policy issue papers. The Alliance sponsors an annual Advocacy Conference.

Ovarian Cancer Research Fund, Inc. (OCRF)
(800) 873-9569
www.ocrf.org
14 Pennsylvania Plaza, Suite 1400
New York, NY 10122

The OCRF is devoted to the formation of early diagnostic treatment programs and research toward the ultimate conquest of ovarian cancer. As OCRF strives to find a cure, it also provides educational outreach programs and public awareness projects, including videos about ovarian cancer and resource materials.

Ovarian Plus: Gynecologic Cancer Prevention Quarterly
nceil@kona.net
www.monitor.net/ovarian

The newsletter has timely information about international research, diagnosis, and treatments for ovarian cancer and other gynecologic cancers. It targets risk reduction, screening, early detection, psychosocial and policy issues, and addresses current events in the ovarian cancer community.

Ovarian Problems Discussion List
www.acor.org

The Ovarian Problems Discussion List is an e-mail support group. To subscribe, browse through the many cancer lists there until you get to ours—you can subscribe online. You can also subscribe through e-mail: send mail to: listserv@listserv.acor.org leave the subject line blank or put a dash message: subscribe ovarian Your First Name Your Last Name (an example of the message: subscribe ovarian Jane Doe).

SHARE: Self-Help for Women with Breast or Ovarian Cancer

(866) 891-2392

www.sharecancersupport.org

1501 Broadway, Suite 704A

New York, NY 10036

SHARE is a not-for-profit organization providing information hotlines for breast and ovarian cancer in English and Spanish; peer led support groups; and wellness, education, and advocacy programs. SHARE contributes to awareness regarding research, prevention, and early detection.

Society of Gynecologic Nurse Oncologists (SGNO)

(800) 230-1064

www.sgno.org

Society of Gynecologic Oncologists (SGO)

(312) 235-4060

www.sgo.org

230 W. Monroe, Suite 710

Chicago, IL 60606

The SGO provides referrals to gynecologic oncologists.

Talking it Ovar

(888) OVARIAN

Talking it Ovar is a telephone support program for those dealing with a diagnosis of ovarian cancer, sponsored by the National Ovarian Cancer Coalition, Inc.

The Wellness Community

(888) 793-WELL

www.thewellnesscommunity.org

919 18th Street NW, Suite 54

Washington, DC 20006

The Wellness Community provides free psychosocial support to people fighting to recover from cancer as an adjunct to conventional medical treatment.

Women's Cancer Network

www.wcn.org

The Women's Cancer Network is an interactive internet site that offers understandable medical information about gynecological cancers, treatment options, and experimental programs. By answering specific questions a woman will be told her risk for developing specific cancers such as gynecologic, breast, and colon cancers, and how to change those risks.

The publishers gratefully acknowledge the guidance of the National Ovarian Cancer Coalition, Inc. (NOCC) in constructing this list of resources for ovarian cancer patients.

APPENDIX 2

National Cancer Institute- Designated Comprehensive Cancer Centers

ALABAMA

UAB Comprehensive Cancer Center
University of Alabama at Birmingham
(800) UAB-0933

Chao Family Comprehensive Cancer Center

University of California at Irvine
(714) 456-6310

ARIZONA

Arizona Cancer Center
University of Arizona
(800) 622-COPE

UCSF Cancer Center & Cancer Research Institute

University of California San Francisco
(800) 888-8664

CALIFORNIA

City of Hope National Medical Center
(800) 826-HOPE

COLORADO

University of Colorado Cancer Center
(800) 425-2288

Rebecca and John Moores UCSD Cancer Center

University of California at San Diego
(858) 534-7600

CONNECTICUT

Yale Cancer Center
Yale University School of Medicine
(203) 785-4095

Jonsson Comprehensive Cancer Center

University of California Los Angeles
(310) 825-5268

DISTRICT OF COLUMBIA

Lombardi Cancer Research Center
(202) 444-4000

USC/Norris Comprehensive Cancer Center

University of Southern California
(800) USC-CARE

FLORIDA

H. Lee Moffitt Cancer Center & Research Institute

University of South Florida
(888) MOFFITT or (888) 663-3488

ILLINOIS

Robert H. Lurie Comprehensive
Cancer Center
Northwestern University
(312) 908-5250

IOWA

Holden Comprehensive
Cancer Center
The University of Iowa
(319) 356-4200

MARYLAND

The Sidney Kimmel Comprehensive
Cancer Center at Johns Hopkins
(410) 955-5222

MASSACHUSETTS

Dana-Farber/Harvard Cancer Center
Dana-Farber Cancer Institute
(866) 408-3324

MICHIGAN

Comprehensive Cancer Center
University of Michigan
(800) 865-1125

The Meyer L. Prentis Comprehensive
Cancer Center of Metropolitan
Detroit; Barbara Ann Karmanos
Cancer Institute
Wayne State University
(800) 527-6266

MINNESOTA

University of Minnesota
Cancer Center
(612) 624-8484

Mayo Clinic Cancer Center
Mayo Foundation
(507) 284-2111

NEW HAMPSHIRE

Norris Cotton Cancer Center
Dartmouth-Hitchcock Medical Center
(800) 639-6918

NEWYORK

Cancer Research Center
Albert Einstein College of Medicine
(718) 430-2302

Roswell Park Cancer Institute
(716) 845-2300

NYU Cancer Institute
New York University Medical Center
(212) 263-8950

Memorial Sloan-Kettering
Cancer Center
(800) 525-2225

Herbert Irving Comprehensive
Cancer Center
College of Physicians and Surgeons
Columbia University
(212) 305-8602

NORTH CAROLINA

UNC Lineberger Comprehensive
Cancer Center
University of North Carolina at
Chapel Hill
(919) 966-3036

**Duke Comprehensive Cancer
Center**

Duke University Medical Center
(919) 416-3853

**Comprehensive Cancer Center
Wake Forest University**
Bowman Gray School of Medicine
(800) 446-2255

OHIO

Ireland Cancer Center
Case Western Reserve University and
University Hospitals of Cleveland
(800) 641-2422

**Arthur G. James Cancer Hospital
& Richard J. Solove Research
Institute**
Ohio State University
(800) 293-5066

PENNSYLVANIA

Abramson Cancer Center
University of Pennsylvania
(800) 789-7366

Fox Chase Cancer Center
(888) 369-2427

**University of Pittsburgh Cancer
Institute**
(800) 237-4724

TENNESSEE

Vanderbilt-Ingram Cancer Center
Vanderbilt University
(800) 811-8480

TEXAS

**The University of Texas
M. D. Anderson Cancer Center**
(800) 392-1611

San Antonio Cancer Institute
(210) 567-2710

VERMONT

Vermont Cancer Center
University of Vermont
(802) 656-4414

WASHINGTON

**Fred Hutchinson Cancer Research
Center**
(206) 288-1024

WISCONSIN

Comprehensive Cancer Center
University of Wisconsin
(800) 622-8922